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American Medical Association
Council on Pharmacy &
Chemistry

ANNUAL REPRINT OF THE REPORTS

OF THE

COUNCIL ON PHARMACY AND CHEMISTRY

OF THE

AMERICAN MEDICAL ASSOCIATION

FOR 1919

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COMMENTS THAT HAVE APPEARED
IN THE JOURNAL

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PREFACE

This volume—the Annual Reprint of the Reports of the Council on Pharmacy and Chemistry of the American Medical Association—contains the reports of the Council that have been adopted and authorized for publication during 1919. It includes reports of the Council previously published in THE JOURNAL, along with such editorial comments as have accompanied them. In addition, the volume contains reports of the Council which, because of their lesser importance, were not published in THE JOURNAL, and which as a matter of record are included here. That the Council's official reports may be made available to physicians, chemists, pharmacologists and others interested in medicine, the Council authorized publication of this volume.

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REPORTS OF THE COUNCIL ON PHARMACY AND CHEMISTRY

HAVENS' WONDERFUL DISCOVERY

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., March 27, 1919, p. 883

The following report has been authorized for publication by the Council.

W. A. PUCKNER, Secretary.

E. C. Havens, Sioux Falls, S. D., requested an examination of a remedy which he asserts he discovered for the cure of influenza. The labels of the specimens submitted read:

"Prof. E. C. Havens'
Wonderful Discovery
INFLUENZA PREVENTIVE

"Directions—Take ½ teaspoonful in wine glass of water not over twice a day for one week, then repeat every alternity week.

"This remedy is good for Coughs, Colds, Lung Diseases, LaGrippe, Influenza, Rheumatism; good for Pains, Cramps, Backache, Lumbago, Neuralgia; for severe pains soak your feet in hot water for 3 nights, add 3 tablespoons of baking soda in water and apply Anti-Flue Medicine to the affected parts.

"This is manufactured and sold by Prof. E. C. Havens, formerly of New York, branch office now located Main Ave. and 10th St., Sioux Falls, S. D. Official Rules of the Council on pharmacy and chemistry of the American Medical Association shall be complied with."

In response to a statement asking for the composition of the "remedy" and for evidence for the claimed curative virtues, Mr. Havens sent the following "formula" and testimonials:

Havens' Rheumatic Remedy

Oil Wintergreen	2 drams
Oil Sassafras	2 drams
Oil Black Pepper	2 drams
Spts. Camphor	1 dram
Spts. Turpentine	2 drams
Spts. Chloroform	1 dram
Tr. Arnica	1 dram
Tr. Opium (out)	1 dram
Alcohol	8 ounces

The following is typical of the testimonials:

"Prof. Havens' Discovery for the cure of Influenza has, to my personal knowledge, done wonders for those who have used it. I personally know of several very severe cases which it has cured and of many

cases which have been prevented by its use. I am taking the medicine as a preventative and can honestly say that I am glad of the opportunity of securing it.

I think the people should know more about this discovery during these times."

When inquiry was made if the formula for "Havens' Rheumatic Remedy" represented the composition of "Prof. E. C. Havens' Wonderful Discovery," and if the word "out" written after tincture of opium meant that this ingredient was not now a constituent of the preparation, Mr. Havens wrote:

"In response to your letter of the 30th ult., beg to state that the Opium is not necessarily an ingredient in the compounding of this remedy, as it is difficult to obtain and I have eliminated its use.

"This formula for Havens' Rheumatic Remedy is the same formula as is used in Prof. E. C. Havens' Wonderful Discovery. I discovered the virtues of the remedy in the treatment of Influenza by practical experience and hence the name 'Discovery.'"

The Council finds that E. C. Havens' Wonderful Discovery is an unscientific, irrational mixture, marketed under therapeutic claims which are unwarranted and without foundation. As the preparation is irrational and unscientific, the promise "Official Rules of the Council on Pharmacy and Chemistry of the American Medical Association shall be complied with" is obviously false.

COLLOSOL COCAINE NOT ADMITTED TO N. N. R.

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., April 12, 1919, p. 1094

The report which appears below was adopted by the Council and sent to the Anglo-French Drug Co., Ltd., New York, for comment in December, 1918. No explanation has been received from the manufacturer. For the information of the profession the Council has now authorized publication of the report.

W. A. Puckner, Secretary.

"Collosol Cocaine" was submitted to the Council in October, 1918, by the Anglo-French Drug Co., Ltd., New York, under the claim that it was an "absolute colloid" and that it contained "1 per cent. cocain." The label on the submitted specimen declares:

"Collosol Cocaine 1-100"

". . . the Cocaine exists as the pure alkaloid in the Colloidal state—the condition in which it is isomorphic with the protein of the body fluids. The effect is more prolonged than that of a molecular Cocaine Solution and being *non-toxic* absorption presents no practical danger."

The product was assigned to the Committee on Pharmacology for consideration. The following report was submitted and its adoption by the Council recommended by the committee:

> "Collosol Cocaine" is said to be a colloidal form of cocain and is alleged to possess a remarkably low toxicity. The subjoined report of the A. M. A. Chemical Laboratory, however, shows that the preparation does not have the composition claimed for it and it is, in effect, misbranded. In fact the English manufacturers concede that it is not an "absolute colloid" and that the declaration with regard to the percentage of cocain is incorrect.
>
> It is recommended that, without considering other conflicts with the rules of the Council at this time, "Collosol Cocaine" be declared inadmissible to New and Nonofficial Remedies for conflict with Rule 1 which requires that the composition of an article must be correctly declared. The report of the A. M. A. Chemical Laboratory is appended.

REPORT OF THE A. M. A. CHEMICAL LABORATORY

Simpson, Hewlett, and Eyre (*Lancet,* April 28, 1917, p. 660) reported "Collosol Cocaine" to be much less toxic than cocain. These writers, however, did not verify the statements as to composition and in the light of subsequent chemical examination it is not to be wondered at that "Collosol Cocaine 1.0 per cent." was much less toxic than a solution containing 1.0 per cent. of cocain hydrochlorid.

Barger, Dale and Durham report from the Department of Biochemistry and Pharmacology, Medical Research Committee (*Lancet,* Dec. 1, 1917, p. 825), that they examined "Collosol Cocaine" and found it to contain but 0.25 per cent. of cocain. They also found that the cocain was not present in a colloidal form. Discussing the low toxicity claimed by the manufacturers, these investigators state:

> "In the samples which we examined the toxicity was, indeed, much lower than that of an ordinary 1 per cent. solution of a cocain salt; but the local anesthetic action was low to a corresponding degree, and both actions corresponded satisfactorily with the proportion of cocain chemically recoverable from the solution."

Stroud, of the Crookes Laboratory (which manufactures the preparation), who apparently had been informed of this work in advance of publication, admits the correctness of it, and states (*British Medical Journal,* Nov. 24, 1918, p. 710) that "whilst the colloidal protective apparently absorbs a portion of the cocain, the remainder is found not to exhibit the attributes of a colloid. . . ."

The specimen of "Collosol Cocaine" submitted to the Council and labeled "Collosol Cocaine 1-100" was found to contain at most 0.4 per cent. cocain. The examination was made

in accordance with the method used by Barger, Dale and Durham and calculated as cocain. This method, however, probably would not distinguish between cocain and basic decomposition products, but would include all as cocain in the amount found. The specimen of "Collosol Cocaine" examined was neutral or slightly acid, a fact which tends to confirm the conclusion of the British investigators that "Collosol Cocaine" contains cocain in noncolloidal form and precludes an increased physiologic effect due to alkalinity.

The Council adopted both the report submitted by the committee and also that of the A. M. A. Laboratory and declared "Collosol Cocaine" inadmissible to New and Nonofficial Remedies.

CUPRASE NOT ADMITTED TO N. N. R.

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., April 12, 1919, p. 1095

The Council has authorized publication of the following report on Cuprase, sold by the Anglo-French Drug Co., Ltd. The Council's criticisms of the advertising claims were sent to the firm, December, 1918. The firm made no reply and essentially the same claims are contained in recent advertisements.

W. A. Puckner, Secretary.

"Cuprase" is now being advertised and sold in the United States by the Anglo-French Drug Co., Ltd., the firm which also markets it in England. It is said to be "prepared in the Laboratories of F. Ducatte, 8 Place de la Madeleine, Paris." According to an advertising circular entitled "The Medical Treatment of Cancer" "Cuprase" is "chemical colloidal copper"; in another place it is "a colloidal copper hydroxid," which is said to be obtained chemically by the reduction of salts of copper in the presence of albumosic acid.

A box (price $8.50 less 10 per cent. discount) of "Cuprase-Doctor Gaube du Gers" was purchased recently from the Anglo-French Drug Co., Ltd. It contained eight ampules each containing approximately 6 c.c. of a brownish fluorescent liquid. No information of composition was given on the box, except the line: "Chaque ampoule contient: 0 gr. .00121 de Cuivre pur" (Each ampule contains 0.00121 gr. of pure copper). The A. M. A. Chemical Laboratory reports that the preparation does contain a small amount of copper, with some protein material and about 1 per cent. sodium chlorid.

The therapeutic claims in the advertising circular are those commonly made for cancer "cures" and are about equally convincing. The publication of such statements and quotations as the following, which appear in a pamphlet "The Medical Treatment in Cancer," cannot be too strongly condemned in a medicament that at best has only an experimental status:

"A special preparation, Cuprase, has been introduced into therapeutics which has been remarkably successful. In the history of the therapeutics of cancer, nothing has been found which can compare with the effects produced by means of Cuprase. Clinical facts carry greater weight than theoretical deductions. It follows, from the clinical observations which I have collected, that in the large majority of cases Cuprase effects the diminution or disappearance of the pains, an improvement in the general condition, a diminution or arrest of the neoplasms, and finally in certain cases, a cure has been effected. It should be remarked that all or nearly all the observations refer to inoperable cases in which the prognosis was unfavorable at an early date. It is needless to emphasize the practical importance of a preparation capable of yielding such results, even relative, in the worst stages of a disease which has always been regarded as absolutely resisting the action of all internal remedies."

"To sum up, Cuprase has given positive results in about 94 per cent. of the cases in which it has been employed for a sufficiently long period, and some brilliant results in about 20 per cent. of these cases. Therefore, it may be affirmed, that among the internal remedies for cancer, Cuprase is the one which has produced the most successful results, and can, under certain circumstances, compete with surgical methods, even, so far as the rapidity of their results are concerned."

"It is indicated:

(a) apart from all operation, and as a specific and curative remedy;
(b) before an operation, in order to give tone to the patient, mobilise the tumour, destroy its toxins;
(c) after the operation, as a tonic and anti-toxic, and in order to avoid frequent relapses which are always possible."

Essentially the same statements are made in the more recent advertisements (f. i. Urological and Cutaneous Review, Feb., 1919). Opposed to these loose statements are the results of Richard Weil (The Journal A. M. A., 1913, Sept. 27, p. 1034; ibid, 1915, April 17, p. 1283). Weil avoided pitfalls of subjective impressions and used as the essential criterion of efficiency "the demonstrable reduction in size of a tumor, of a kind not to be attributed to the natural processes of evolution of that tumor or of its associated lesions" (l.c. 1915, p. 1289).

The available evidence for Cuprase is far from meeting this criterion. That published by the manufacturers and agents presents only vague generalities, and no definite data. The evidence gathered by Weil himself permits an estimate of the value of Cuprase and it is entirely unfavorable. He states (l.c. 1915, p. 1288):

"Colloidal copper has been used in recent time for the same purpose by Gaube du Gers and by others. I have recently examined the effects of colloidal copper on malignant tumors in man, and have been unable to find that it has any therapeutic value. Furthermore, a study of the distribution of the copper in tumors obtained at operation or by necropsy from individuals so treated failed to show that the copper had been deposited therein."

In view of the extravagant and cruelly misleading therapeutic claims, and the indefinite statements of composition, the Council voted Cuprase ineligible to N. N. R., and authorized the publication of this report.

ANNUAL MEETING OF THE COUNCIL ON PHARMACY AND CHEMISTRY

From The Journal A. M. A., April 26, 1919, p. 1243

The Council on Pharmacy and Chemistry, at its recent annual meeting, discussed at length the revision of New and Nonofficial Remedies and the problems of investigating proprietary articles, both of those voluntarily submitted to the Council, and also of those which the Council takes up on its own initiative. Other subjects of special interest to the medical profession, that were considered and acted on at this meeting, were:

Nonspecific Protein Therapy.—The Council decided to publish, at an early date, a report on the unscientific and commercial propaganda which is being conducted in the interest of establishing the use of therapeutic agents of this character. The Council believes that the profession should be warned of the specious and unproved arguments which are being circulated concerning the results obtained from preparations of this character.

Serums and Vaccines.—The Council appointed a committee to study the problems of serum and vaccine therapy. This, to the end that it might publish in THE JOURNAL for the information of the medical profession, the evidence obtainable regarding both the value of, and also the dangers incident to, the use of serums and vaccines. The study is to include (*a*) an exhaustive review of the literature; (*b*) a tabulation of the experiences of the Army and Navy as revealed in available official reports, and (*c*) a review of the data relative to these therapeutic agencies available in various clinics of scientific standing.

Hay Fever Pollen Extracts.—A special committee was appointed to study and report on the present status of pollen extracts in the prophylaxis and treatment of hay fever. This investigation is to include, especially, the rationale of the pollen protein mixtures now being advertised.

Supervision of Potent Drugs by the U. S. Public Health Service.—The Council adopted a resolution urging the enactment of a law by Congress which shall require the Public Health Service to extend its present work of testing the toxicity and efficiency of serums, vaccines, toxins, and antitoxins, to cover that of testing and standardizing other potent remedies that are used hypodermically or intravenously. The selection of such products as are a source of special danger to the public health, unless standardized and tested as to toxicity, would be left to the judgment of the Surgeon-General of the Public Health Service. Some of the preparations which might call for such standardization and testing are extracts of glands such as the pituitary gland, etc., and highly toxic drugs, such as arsphenamine, neoarsphenamine, digitalis preparations, etc.

Arsphenamine.—The Council passed this resolution: "That the control of the purity and potency of arsphenamine by the Public Health Service shall be continued after the conclusion of peace, and the control of the price be placed under an appropriate government agency."

Articles Described, But Not Accepted.—The Council has long recognized that there are proprietary preparations of therapeutic value which are so exploited as to be inadmissible to New and Nonofficial Remedies. The claims made for such preparations are unproved and, in many instances, are palpably false, and such claims and other violations of the rules of the Council make the acceptance of the products impossible. The Council decided to describe, for the information of physicians, articles of this character, and at the same time to give the reasons which stood in the way of including these preparations in N. N. R. The Council further requested that descriptions of articles of this character might be published in THE JOURNAL, and decided that these descriptions should later be published in a separate section of New and Nonofficial Remedies.

Cooperation in the Teaching of Pharmacology and Therapeutics.—A committee on Education was appointed to revive the pre-war work of the Council in establishing fuller cooperation between the Council and the teachers of therapeutics and pharmacology in medical schools. The object in view is that of bringing to the attention of third- and fourth-year

medical students the therapeutic and pharmacologic problems which beset the young practitioner and showing the value of the Council's work in helping the profession to solve these difficulties.

Radium Water Therapy.—Another committee whose report should prove instructive and important is that appointed to investigate the present status of the therapeutic value of radium water therapy.

The following members of the Council on Pharmacy and Chemistry were in attendance:

C. L. Alsberg, Chief of the Bureau of Chemistry, U. S. Department of Agriculture.

R. A. Hatcher, Professor of Pharmacology, Cornell University Medical College.

John Howland, Professor of Pediatrics, Johns Hopkins University Department of Medicine.

Reid Hunt, Professor of Pharmacology, Harvard University Medical School.

Henry Kraemer, Professor of Pharmacognosy, University of Michigan, College of Pharmacy.

W. T. Longcope, Bard Professor of the Practice of Medicine, College of Physicians and Surgeons of Columbia University.

G. W. McCoy, Director of the Hygienic Laboratory, U. S. Public Health Service.

F. G. Novy, Professor of Bacteriology, University of Michigan.

W. W. Palmer, Associate Professor of Medicine, College of Physicians and Surgeons of Columbia University.

W. A. Puckner, Secretary of the Council on Pharmacy and Chemistry and Director of the Chemical Laboratory of the American Medical Association.

L. G. Rowntree, Professor of Medicine, University of Minnesota.

G. H. Simmons, Chairman of the Council, and Editor of The Journal of the American Medical Association.

Torald Sollmann, Professor of Pharmacology and Materia Medica, Medical Department, Western Reserve University.

Julius Stieglitz, Vice-Chairman of the Council, and Professor of Chemistry, University of Chicago.

W. A. Puckner, Secretary.

COLLOSOL PREPARATIONS

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., June 7, 1919, p. 1694

The Council has adopted and authorized publication of the report which appears below declaring "Collosol Argentum," "Collosol Arsenicum," "Collosol Cocain," "Collosol Cuprum," "Collosol Ferrum," "Collosol Hydrargyrum," "Collosol Iodin," "Collosol Manganese," "Collosol Quinin" and "Collosol Sulphur" inadmissible to New and Nonofficial Remedies, because their composition is uncertain (conflict with Rule 1). In the few cases in which the therapeutic claims

for these preparations were examined, the claims were found to be so improbable or exaggerated (conflict with Rules 6 and 10) as to have necessitated the rejection of these products.

W. A. PUCKNER, Secretary.

The Anglo-French Drug Co., Ltd., London and New York, in November, 1918, requested the Council to consider the products "Collosol Argentum," "Collosol Arsenicum," "Collosol Cocain," "Collosol Cuprum," "Collosol Ferrum," "Collosol Hydrargyrum," "Collosol Iodin," "Collosol Manganese," "Collosol Quinin" and "Collosol Sulphur." The term "Collosol" appears to be a group designation for what are claimed to be permanent colloidal solutions, marketed by the Anglo-French Drug Co., Ltd. Were this claim correct, "Collosols" should contain their active constituents in the form of microscopic or ultramicroscopic suspensions, protected against spontaneous precipitation by the presence of proteins or some similar "stabilizers."

According to the original patent specifications for Collosols, the metals are precipitated or treated with "peptone," which acts as the suspending or stabilizing agent. The method of using the peptone makes it doubtful, in the first place, whether the major part of the metals is present in colloidal form, or merely in the form of peptonates, i. e., as ordinary salts. Moreover, the later patents indicate that the products have been unsatisfactory; "experience having shown that some metal colloids under certain conditions not yet fully understood have the tendency to break down after a certain period" (U. S. patent No. 1,116,247). Phenol, it is claimed, has a tendency to counteract this decomposition, and the patent covers the use of phenol for this purpose.

It is difficult to see how phenol could possibly have such action. In fact, it obviously does not, for a number of the samples of Collosols submitted to the Council had separated. For instance, "Collosol Hydrargyrum" was not a colloidal solution at all, but a suspension of a coarse powder. The ampules of "Collosol Ferrum" contained a considerable quantity of flocculent precipitate. If either of these preparations were injected intravenously as directed, death might result, making the physician morally if not legally liable.

The recklessness of the claims is further illustrated by the advice that these indefinite mixtures of poisonous metals can be injected in unlimited quantities. Thus, Henry Crookes stated (*Chemical News,* May 7, 1914, p. 218) that Collosols "contain so small a proportion of metal, viz., 1 in 2000, that even a poisonous body like arsenic can be used with

impunity." He stated that they may be applied as a lotion, intramuscular or intravenous injection, and that "one pint or more can be injected intravenously."

In the case of "Collosol Cocain," as was brought out in the Council's report published in THE JOURNAL, April 12, 1919, the manufacturers have admitted that the product is not what they have claimed—and still claim—for it. The report of the A. M. A. Chemical Laboratory showed that "Collosol Cocain," instead of containing 1 per cent. cocain as claimed, contained, in fact, at most not more than 0.4 per cent. cocain.

The report of the A. M. A. Chemical Laboratory on the Collosol products was sent by the Council to the New York office of the Anglo-French Drug Co., Ltd., in duplicate, in order to facilitate reference to the London office. This was some months ago. The information which the Council requested has not yet been received, nor has the Anglo-French Drug Co., Ltd., indicated its intention of supplying such information. On the other hand, claims to which specific objection have been made, continue to appear in current advertising. Accordingly, the Council authorizes publication of this report, and declares the Collosol preparations previously named ineligible to New and Nonofficial Remedies.

Additional Notes on Collosol Evidence

In addition to the preceding the following notes of the referee on the evidence so far submitted were sent to the Anglo-French Drug Company, Ltd., for consideration:

Collosol Iodine: The leaflet which describes Collosol Iodine contains claims that are improbable, not in accord with accepted facts nor substantiated by evidence; for instance:

"This preparation contains Iodine in its most active form . . ."

"The disadvantages of 'iodism' and nausea frequently associated with iodides never occur with Collosol Iodine."

"In the case of Colloidal Iodine the whole of the Iodine is absorbed and enters into molecular combination with protein to form an iodo-amino acid and . . . exerts a reducing action on the lipoids producing a different condition of the blood—hence the use of Iodine as an 'alterative'."

"Intravenously the action of Collosol Iodine is more rapid . . . in cases of pyemia . . . thus showing its absolute non-toxicity."

" 'Per se' Collosol Iodine is only slightly parasitotropic and bacteriotropic but micro-organisms are very greatly influenced by its action, and not only is the effect of a subsequently administered remedy greatly increased but also the insoluble colloidal protein of serum itself is reduced to smaller particles, thus increasing its surface and adsorptive capacity and consequent germicidal power. In some cases the serum, thus aided, is enabled to throw off a milk microbial invasion. The above action can be readily demonstrated 'in vitro' by means of the ultra-microscope."

"In Cancer, the intravenous injection of Collosol Iodine relieves pain, even where large dosage of morphine is ineffective."

"In Rheumatism the ionic method of treatment with Collosol Iodine is strongly advised."

"In Recovery from Alcoholism the internal administration of Collosol Iodine restores the normal condition of cell activity, ensuring rapid recovery."

Collosol Hydrargyrum: This is said to be a preparation of colloidal mercury and would therefore be similar to Electromercurol (New and Nonofficial Remedies, 1919, p. 167). Colloidal mercury preparations have been used to some extent; they appear to have no decided advantage over other, noncolloidal, mercury compounds. They differ sufficiently from them, however, to justify acceptance for New and Nonofficial Remedies, providing that reasonable claims are made for them. The leaflet advertising Collosol Hydrargyrum contains statements that cannot be accepted and require thorough revision to make them acceptable. The following are instances:

"Although—especially locally—the action of mercurials is markedly antiseptic, when taken internally or injected, it has been stated by some of the best known authorities, that their action is rather to increase the natural resisting power of the body to disease, probably because of stimulation of the oxidases."

With the soluble mercurials "considerable upset of the normal cell conditions of the tissues ensues whilst these soluble salts are being converted to a condition in which the body can make use of them."

"The colloidal state . . . is stated by some authorities in the case of mercury to be invariably precedent to absorption . . . With the usual forms of mercury the danger of too great a dose per cell is considerable, but in the case of colloidal mercury, the diffusion is extremely rapid and chemical affinity low. Hence the danger to the individual leucocyte is minimized and the maximum effect obtained."

". . . absence of pain is usual in the administration of colloidal preparations and is due to their isomorphism with the colloidal lipoid and protein of the tissues and body fluids."

"According to McDonagh, . . . mercury acts as an oxidizing agent and that the process of oxidation is more effective in the early stages of syphilis in producing the death of the causal organism . . ."

Collosol Manganese: The circular submitted to the referee is a reprint of a paper by Sir Malcolm Morris on "The Treatment of Furunculosis and Other Deep-Seated Coccogenic Infections by Collosol Manganese." It reports four cases of furunculosis, each of which cleared up after the intramuscular injection of a few doses of Collosol Manganese. The author seems to attribute the cure to the manganese but the evidence is not convincing. Even the author admits that, in the treatment of furunculosis in general "when at last the dismal procession ends, this often appears to be less the result of treatment than because the disease has run its natural course." Unless much better evidence is in existence,

the preparation must be considered to conflict with Rule 6, which requires therapeutic claims to be substantiated.

Collosol Argentum: The evidence submitted as to actions consists of a single reprint by Roe, which is not convincing, and this fantastic statement by Boys:

"A young girl, aged 18, came to my house with acute inflammation of one eye with an ulcer on the cornea. Two drops of Collosol Argentum were dropped in the eye at 7 p. m., and a pad placed over the eye. When she came next morning the eye was quite well; the ulcer had disappeared, and there was no inflammation."

There is no evidence that this preparation acts as catalyzer and assists the natural resisting bodies of the tissues; or that these are "oxygen carriers." Unless the claims are supported by better evidence, they, in the opinion of the referee, could not be accepted.

There have been submitted to the Council samples of the following metallic Collosols:

Collosol Argentum	Collosol Ferrum
Collosol Arsenicum	Collosol Hydrargyrum
Collosol Cuprum	Collosol Manganese

Also Collosols of Iodine and Sulphur, and finally Collosols of Cocain and Quinin. Of all the above, except sulphur, only three small ampules have been submitted. This does not admit of any chemical examination but a statement of the physical appearance may be of interest.

Collosol, Arsenicum, 0.2 *per cent.:* Very turbid with large quantities of a lemon yellow floculent precipitate. On shaking does not become homogeneous and rapidly separates again.

Collosol Argentum, 1-2000: The liquid has a slight opalescence. There is considerable deposit of a heavy black precipitate. Does not become homogeneous on shaking and the black substance quickly separates again.

Collosol Cuprum, 0.5 *per cent.:* Dark red somewhat opalescent liquid. No precipitate. May be colloidal.

Collosol Ferrum, 1-2000: Liquid clear. Large quantities of dark brown flocculent precipitate. The precipitate is not distributed evenly when the mixture is shaken and settles out quickly on standing.

Collosol Hydrargyrum, 5 *per cent.:* Milky liquid. Large quantities of white deposit mixed with considerable black. The deposit mixes fairly well but the greater part settles out after standing an hour or two.

Collosol Manganese, 2.5-1000: Clear reddish-brown liquid without deposit of any kind. Is not opalescent or fluorescent.

Collosol Iodin, 1-500: Very pale straw colored liquid without deposit. Has a slight opalescence.

Collosol Sulphur, 1-100: Liquid is opalescent. There is some deposit of yellow particles. A four ounce bottle was also submitted. The liquid in this bottle is milky with considerable deposit of yellow crystals like ordinary crystalline sulphur.

Collosol Cocain, 1-100: Transparent, colorless liquid with no deposit. Chemical examination showed 0.4 per cent. of what may have been cocain. This residue gave akaloidal tests.

Collosol Quinin, 1-100: Slightly opalescent, colorless liquid, with no deposit. Gives alkaloidal reactions.

PULVOIDS CALCYLATES COMPOUND

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., June 14, 1919, p. 1784

The Council has authorized publication of the following report, not so much because the preparation with which it deals is of any great importance, but as a protest against the large number of similar irrational complex mixtures which are still offered to physicians.

W. A. Puckner, Secretary.

Pulvoids Calcylates Compound (The Drug Products Co., Inc.) are tablets each of which is claimed to contain:

"Calcium and Strontium Disalicylate, 5 grs.; Resin Guaiac, ½ gr.; Digitalis, ¼ gr.; Cochium [colchicum?] Seed, ¼ gr.; Squill, ¼ gr.; Cascarin, 1/16 gr. with aromatics."

"Pulvoids Calcylates Compound (Sugar coated orange color)" is advertised (*Medical Times,* January, 1919) as being "Analgesic-Antipyretic and Diuretic," and is included in the preparations designated by the advertiser as "Approved Remedies for LaGrippe and 'Flu.'" The claim that "Their tolerance is remarkable" refers not to the physicians who tolerate such products, but to the alleged fact that Pulvoids Calcylates are tolerated remarkably well. The advertisement continues:

"May be given persistently and continuously without gastric disturbances."

"They are uniformly efficient. More certain in effect than the ordinary Salicylates."

It would be difficult to find an advertisement of equal length containing a greater number of misleading or directly false statements than are found in this one. The Journal (April 22, 1916, p. 1307) has called attention to the lack of justification for this absurd mixture of drugs and has dis-

cussed the preparation with especial reference to its use in acute rheumatism, in which the salicylates occupy a special field. The advertisement just quoted mentions La Grippe and "Flu" (or Influenza) as special fields of usefulness for this preparation. This, apparently, is merely an attempt to spread the sail for any breeze. Salicylates have a field of usefulness in influenza in that they often afford relief from pain. There is no reason to suppose that a mixture containing calcium and strontium salicylates—the "Calcium and Strontium Disalicylate" of Pulvoids Calcylates is probably a mixture of calcium and strontium salicylate[1]—has any greater salicylic effect than an equal amount of sodium salicylate. On the other hand, it is worse than useless to give colchicum, squill and digitalis for the relief of such pains.

Should cardiac dilatation develop, and digitalis medication be required it would be impossible to adjust the dose of such a mixture with special reference to the digitalis action, which alone would be indicated for that condition. No educated physician at present would think of giving resin of guaiac merely because his patient required digitalis, nor would he administer "cascarin," whatever that may be, in fixed doses, every time he gave a dose of a salicylate.

It is impossible to recognize the several effects induced by this therapeutic omneity, and the medical profession should consider it an insult to be offered mixtures such as Pulvoids Calcylates Compound.

Pulvoids Calcylates Compound is, per se, of no great importance; it is one of a type. It has been selected as one of the utterly irrational and therefore potentially dangerous mixtures, that may be found by the score or the hundred in the catalogues of practically every pharmaceutical manufacturing firm in the United States.

PROTEOGENS OF THE WM. S. MERRELL COMPANY

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., July 12, 1919, p. 128-30

The Council has adopted and authorized publication of the statement which appears below, declaring Proteogen No. 1 (Plantex) for Cancer, Proteogen No. 2 for Rheumatism, Proteogen No. 3 for Tuberculosis, Proteogen No. 4 for Hay Fever and Bronchial Asthma, Proteogen No. 5 for Dermatoses, Proteogen No. 6 for Chlorosis, Proteogen No. 7 for

1. See report, THE JOURNAL, Sept. 9, 1916, p. 827.

Secondary Anemia, Proteogen No. 8 for Pernicious Anemia, Proteogen No. 9 for Goitre, Proteogen No. 10 for Syphilis, Proteogen No. 11 for Gonorrhea, and Proteogen No. 12 for Influenza and Pneumonia inadmissible to New and Nonofficial Remedies because their composition is secret; because the therapeutic claims made for them are unwarranted; and because the secrecy and complexity of their composition makes the use of these preparations irrational.

The Council took up the consideration of the Merrell Proteogens because of inquiries received, and on January 27 invited the Merrell Company to aid in the proposed investigation by submitting information in regard to the composition of the preparations, submitting the current advertising, and presenting evidence for the claims that were made for the preparations. While the Merrell Company agreed to submit the requested information, this had not been received at the time the report of the referee to whom the products had been assigned (Referee 1), was adopted. This report was sent to the company on April 4. In reply the Merrell Company protested against the conclusions of the report and submitted considerable material in an attempt to support the claims made for the products. This material was examined by the first referee and then transmitted to a second referee (Referee 2) for consideration. The second referee concluded that the matter submitted offered no evidence that would justify the Council in modifying the report first adopted, and hence recommended that its publication be authorized.

In accordance with this recommendation (report of Referee 2), the Council authorized the publication of the reports of both the first and second referees.

W. A. Puckner, Secretary.

Report of First Referee on Proteogens

"Proteogens," according to the William S. Merrell Co., are "Polyvalent Proteins of Non-Toxic Plant Origin." The subject of Proteogens can best be approached by recalling the history of "Autolysin," an alleged remedy for cancer, originated by A. S. Horowitz, Ph.D. This was exploited some years ago, and was finally shown to be worthless. Proteogens are said to be prepared "under the personal supervision of the originator, Dr. A. S. Horowitz." The composition of the different Proteogens is essentially secret. The assertion was made at one time, but is not found in the present advertising matter, that Plantex—now called "Proteogen No. 1"—is similar to Autolysin. Now the Proteogens are said to be "prepared by a special process employing various combinations of plants." Further:

"The biologic principles present are chlorophyll, chromoplast, lipoids and vitamines; these are ferments or enzymes. The vegetable acids, metalloids and metals present in all plants in colloid form act biochemically. Among the metalloids are hydrogen, carbon, manganese, oxygen, sulphur, phosphorus and chlorine; the heavy metals are iron, potassium, sodium, magnesium and copper. These biochemic principles are always present in plants as colloids."

It is claimed by the Merrell Company that:

"Proteogens stimulate the cytogenic mechanism to higher activity; therefore, indirectly cleave the invading microorganism and eliminate their special toxins. Proteogens swing the disturbed metabolism back to normal and, by natural processes, build up effective defenses against recurrent bacterial attacks."

Proteogen No. 1 was first introduced as "Plantex," and at that time the Merrell Company referred to a preparation that was the result of "a series of studies" carried out by a "noted biologist" with a view of "evolving a Cancer remedy" that was "to be autolytic in character," and announced:

"The House of Merrell always interested in the progress of plant therapy, began pharmacological experimentations to reproduce this same substance. The qualitative and quantitative analysis of the substance as used in New York having been published simplified matters. A somewhat similar remedy has now been prepared. It consists of the following substances — Menyanthes trifoliata [Buckbean], Melilotus officinalis [Yellow sweet clover], Mentha crispa [Curled mint], Brassica alba [White mustard], Anemone hepatica [Liver leaf], Viola tricolor [Pansy], Anthemis [Roman chamomile], Fructus colocynthidis [Colocynth], Lignum quassiæ [Quassia] Urtica dioica [Nettle], Radix rhei [Rhubarb root], Hedge hyssop. These substances are in approximately equal proportions with the exception of the mustard which forms 20 per cent. of the mixture, and the colocynth fruit which is 5 per cent."

With respect also to the other Proteogens listed above, study of medical literature revealed no evidence establishing their therapeutic value; in fact, no evidence was found other than that appearing in the advertising matter of the manufacturer. The range of diseases in which Proteogens are recommended is so wide as to make obvious the lack of scientific judgment which characterizes their exploitation. A circular letter, received January, 1919, reminded the physician that about a year ago his attention had been directed to Proteogen No. 1 for cancer, that later developments enabled the firm to recommend for his consideration "a series of Proteogens (Nos. 2 to 9)," and that now "In response to an insistent demand, Dr. A. S. Horowitz has prepared two new Proteogens —No. 10 for Syphilis and No. 11 for Gonorrhea." A postscript to this circular letter announced another preparation, "Proteogen No. 12 for Influenza and Pneumonia," a "develop-

ment out of the present influenza epidemic," and admitted that "It has not had the clinical experimentation that precedes our introduction of a new product."

The introduction of No. 12 was effected by means of a special bulletin which consists exclusively of clinical reports from seven physicians, all from Chicago save one, and all purporting to show most favorable results from No. 12. They describe cases which any physician with experience with influenza can duplicate without any special treatment.

It is difficult to give serious consideration to a set of alleged remedies when the only evidence is that furnished by the proponents of the alleged remedies. This is particularly true when the alleged remedy does not make a sufficient appeal to one's sense of the rational in therapeutics to lead one to feel justified in asking a trial at the hands of careful clinical observers. Considering the grave nature of the diseases for which Proteogens are recommended, particularly cancer, tuberculosis, and pernicious anemia, the want of a rational basis for the method of treatment and the general tenor of the advertising matter, it appears safe to conclude that these agents do not represent any definite advance in therapeutics.

As the use of preparations, secret in composition, and of no established value, is contrary to rational therapy, it is recommended that the Proteogen preparations be declared in conflict with Rules 1, 6 and 10.

Report of Second Referee Reviewing Manufacturers' Reply

The report declaring the Proteogens of the William S. Merrell Company inadmissible to New and Nonofficial Remedies was adopted by the Council, but before publication it was sent to the Merrell Company for such comments as it might desire to make. In due time the reply of the firm was received. It consisted of two volumes bound in limp morocco, each stamped in gold: "Report Proteogen Therapy Requested by the American Medical Association, 1919; The Wm. S. Merrell Company." The first volume contained 79 pages of typewritten material; the second volume contained 76 pages of typewritten material and a number of advertising booklets put out by the Wm. S. Merrell Company, exploiting the Proteogens.

Among the typewritten material was a 14-page report on "Proteogen Therapy" by its originator, A. S. Horowitz. Following this there are several pages devoted to what is termed "a short qualitative description of the ingredients of major

importance in Proteogens." Then follows a page describing the advertising of Proteogens, and the remainder of the two books is devoted to testimonials, lauding the benefit of Proteogens in diseases such as cancer, tuberculosis, rheumatism, asthma, influenza, enlarged prostate, rheumatic endocarditis, syphilis, eczema, psoriasis, diabetes, secondary anemia, gonococcic infections etc. Finally, there are attached samples of advertising pamphlets.

The dissertation by A. S. Horowitz contains little actual information concerning these substances, but is concerned principally with discussion of foreign proteins, "antiferments," "non-specific proteins," "anti-virolins" and speculations on their hypothetical actions and interactions on each other and on the organs of the body and on bacteria. The report contains many questionable statements.

One finds in this report but few definite statements of facts which are known to be accurate or which could be accepted without question. The qualitative description of the proteins and their components is as vague as the previous discussion. The differentiation between the various Proteogens is extremely indefinite; that for Tuberculosis, No. 3 is described as "polyvalent, non-specific protein which rapidly attacks the acid-fast, encapsulated tubercle bacilli"; Proteogen No. 10 for syphilis is said to be a combination of "non-specific plant proteins and different chemicals which has the power to paralyze and destroy living spirochete." It is stated that Proteogens are scientific preparations based on standard ingredients and that the standardization is more accurate than in serums, vaccines or toxins, etc. The report gives no proof of such statements.

The testimonials that are submitted are typical of "reports" that manufacturers are able to obtain from some physicians, to prove the efficacy of almost any preparation in any disease. Each consists, practically, of the opinion of the individual who has employed the Proteogens or the opinion of the patient who has been treated. Few data are given in these reports from which an impartial conclusion might be drawn. A few of the testimonials presented by the William S. Merrell Company follow. The valuelessness of such material as scientific evidence is obvious:

RHEUMATISM:—*Proteogen No. 2.*—The Doctor has one case being treated with No. 2. She has improved so rapidly she cannot express her pleasure, and will continue for some time on the treatments. She is a patient who was confined during the time she suffered from a rheumatic illness, and it seemed to affect her mental condition. This condition is clearing up also, very much to the pleasure of both patient and doctor.—November 27, 1918.

INFLUENZA:—*Proteogen No. 12.*—First day, temperature 102, gave 1 c.c. Proteogen No. 12; second day, temperature 100, gave 1 c.c. Proteogen No. 12; third day, temperature 98.8, gave 1 c.c. Proteogen No. 12, and then discharged the case as recovered.—October 31, 1918.

ASTHMA:—*Proteogen No. 4.*—Splendid results obtained from a sample of Proteogen No. 4. Three ampoules affected [effected?] complete recovery.—October 9, 1918.

CANCER:—*Proteogen No. 1.*—Mrs. B. pronounced recovered from Cancer by Dr. O. W. A., of Catlin, after having injections of Proteogen No. 1 for some time.—October 4, 1918.

ECZEMA:—*Proteogen No. 5.*—Tried No. 5 on a patient with eczema, and with happy results. Have not done anything for him for about five months—and he is now at his business. Proteogen No. 5 also RELIEVED HIM OF CONSTIPATION AND WHAT HE CLAIMED A TRAUMATIC STRICTURE OF THE LOWER PORTION OF SIGMOID FLEXURE. He is sure pleased and recommending them to his friends. (Proteogens).—February 17, 1919.

SYPHILIS:—*Proteogen No. 10.*—I am getting such excellent results with the No. 10 Proteogen for Syphilis that I am badly in need of more, as I am treating so many cases. Please send me four dozen C. O. D.—October 9, 1918.

ENLARGED PROSTATE:—*Proteogen No. 1.*—Have used Plantex in four cases, with good results in each case. One of them his father, an elderly man.—April 25, 1918.

LOBAR PNEUMONIA.—*Proteogen No. 12.*—The only case I have used Proteogen No. 12, was a man who had Lobar Pneumonia of left lung following Influenza. After crisis came, patient continued to have slight rise in temperature, cough, and after using 10 doses of your Proteogen No. 12, temperature was normal, cough very much better, patient began to take on flesh and is still improving.—December 26, 1918.

TUBERCULOSIS:—*Proteogen No. 3.*—The Doctor writes: The Proteogen No. 3 sent me worked wonders in my patient. The case came under my care when he was too far gone for anything to benefit him a great deal, but the Proteogen did for him more than anyone could have expected, yet he died leaving me with a few ampoules to try on the next patient.—September 20, 1918.

GONORRHEAL CYSTITIS:—*Proteogen No. 11.*—My patient has taken two boxes of your Proteogen No. 11 given for gonorrheal cystitis of probably two years' standing and at this writing I consider her almost, if not entirely, cured which I think speaks very highly of your remedy. I expect to use more of your preparations in the future.—April 12, 1919. [This testimonial, either by clerical error, or because the results were considered remarkable, was repeated elsewhere in the material submitted by the Merrell Company.]

ACUTE GONORRHEA: — *Proteogen No. 11.* — Mr. A. E. R., age 65, weight 140 pounds. First attack. Had had no previous treatment. Came to me January 2, 1919. Had discharge, all acute symptoms, burning, etc. Gave seventeen injections of Proteogen No. 11, also mild antiseptic urethral wash. Discharged on February 15, 1919, clinically cured. —April 11, 1919.

EPITHELIOMA OF BUTTOCK:—*Proteogen No. 1.*—I used Proteogen No. 1 on an epithelioma of buttock some six months ago with favorable results and no return of symptoms as yet.—April 13, 1919.

It is obvious that the Proteogen preparations are in conflict with Rules 1, 6 and 10, and should not be admitted to "New and Nonofficial Remedies." It is recommended that the previous action of the Council be allowed to stand and that publication of both reports be authorized.

"ARSENOVEN S. S." AND "ARSENO-METH-HYD"

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Aug. 2, 1919, p. 353

The Council authorizes publication of the following report. This report declares Arsenoven S. S. of the S. S. Products Company and Solution of Arsenic and Mercury (formerly called Arseno-Meth-Hyd) of the New York Intravenous Laboratory, inadmissible to New and Nonofficial Remedies. The Council takes this opportunity to repeat its warning against the abuses—often dangerous—to which patients are frequently subjected when "intravenous therapy" is employed.

W. A. Puckner, Secretary.

Because of inquiries received, the Council took up the consideration of Arsenoven S. S. and Arseno-Meth-Hyd (now sold as Solution of Arsenic and Mercury). The preparations having been referred to a committee for consideration, this committee reported:

ARSENOVEN S. S.

"Arsenoven S. S." is a preparation put out by the S. S. Products Company, Philadelphia. The claims are made that it is "a simplified office treatment for syphilis" and is "a combination of arsenic and mercury for office use, offering maximum efficiency, safety and convenience." According to the company, "Arsenoven S. S." contains Dimethylarsenin 15.4 grains, Mercury biniodid 1/10 grain, Sodium iodid ½ grain. With regard to the identity of "dimethylarsenin" the company claims: "This product is a compound of cacodylic acid similar to sodium cacodylate but with a more pronounced therapeutic action." The committee recommends to the Council that "Arsenoven S. S." be declared inadmissible to New and Nonofficial Remedies because of unwarranted therapeutic claims.

ARSENO-METH-HYD

"Arseno-Meth-Hyd," is sold by the New York Intravenous Laboratory, New York City, for the treatment of syphilis. It comes in three dosages, 2 gm., 1.5 gm., and 0.7 gm., respectively. The claim is made that "Arseno-Meth-Hyd 2 gm." contains "2 gm. (31 grains) of Sodium Dimethylarsenate (Cacodylate), U. S. P., and Mercury Iodid 5 mg. (1/12 grain)" in 5 c.c. of solution. Physicians are told:

"In primary and early secondary case administer Arseno-Meth-Hyd 2 gm. every sixth day and Mercury Oxycyanide .008 (⅛ grain) intravenously between each injection."

"In Tertiary cases and those of long standing alternate with intravenous injection of Sodium Iodid 2 gm."

The following claims are made for the alleged effectiveness and safety of the cacodylate:

"This methyl compound of arsenic has come into almost universal use for syphilis. On account of lack of toxicity an aggressive routine can be carried on. The simple technic and absence of reactions make it most desirable for the regular practitioner. This large dose gives more uniform results both as healing manifestations and negative Wassermanns."

"Much discussion has surrounded the use of the Methyl Compounds of Arsenic and it has been demonstrated beyond doubt that Cacodylate of Soda proves an effective remedy for syphilis provided that it is properly administrated." [*sic*]

"The low toxicity of this Methyl compound of arsenic is remarkable. It is contraindicated only where a decided idiosyncrasy for even small doses of arsenic exists."

These statements are essentially false and misleading. Cacodylate has *not* come into universal use in the treatment of syphilis, nor has its usefulness been "demonstrated beyond doubt." On the contrary, H. N. Cole (THE JOURNAL, Dec. 30, 1916, p. 2012) has shown that doses so large as to produce renal injury were almost totally ineffective against syphilis. Obviously, "effective doses" if such exist, are not harmless. The dosage advised for Arseno-Meth-Hyd may not produce acute toxic symptoms; nevertheless smaller doses have produced nephritic phenomena. The "Arseno-Meth-Hyd" treatment includes the intravenous injection of about ¼ grain of a mercury salt. Although this is less than the usual dose (about 1 grain per week), the mercury is probably more effective than the cacodylate.

The committee recommends to the Council that, because of the unwarranted therapeutic claims, "Arseno-Meth-Hyd" be held inadmissible to New and Nonofficial Remedies.

The Council adopted both reports of the committee and declared "Arsenoven S. S." and "Solution of Arsenic and Mercury" ("Arseno-Meth-Hyd") inadmissible to New and Nonofficial Remedies. The committee's reports on these two products impel the Council again to call attention to the undesirable and dangerous abuses to which "Intravenous Therapy" lends itself. There is a distinct field for the intravenous administration of drugs in those cases in which immediate drug action is necessary, or when the medicament is likely to be changed if absorbed through the ordinary channels. Unless such indications exist, however, intravenous administration involves not only inconvenience and expense to the patient, but what is more important, unnecessary danger. The fact that indiscriminate intravenous adminis-

tration is peculiarly profitable to certain manufacturing houses makes it all the more necessary for the medical profession to be on its guard in this matter.

In this connection it is well worth while to quote the closing paragraph from an editorial on "Intravenous Therapy" that appeared in THE JOURNAL, Nov. 11, 1916. It is as true today as when it appeared:

"Intravenous therapy will be most securely advanced if its employment is restricted to such well defined fields. [As those mentioned above.] These fields can be satisfactorily determined only by a scientific pharmacologic study of the action of these drugs when so administered in animals, as well as in man, under conditions in which the results are carefully controlled. The intravenous method is an impressive one, approaching in preparation almost to that which goes with a surgical operation. The patient is usually interested and impressed by this new, and, to him, mysterious method. There is a psychic element in his reaction to the injection which is not a factor in his reaction to the same drug when given by mouth. The intravenous injection of a complex mixture would appear to be particularly reprehensible. Little is known, as has been stated, of the results to be expected from intravenous therapy, even with simple substances. The use of complex mixtures will without doubt react against the proper use of the method."

After the report on Arseno-Meth-Hyd had been presented to the Council, a letter was received from the New York Intravenous Laboratory announcing that the preparation "Arseno-Meth-Hyd" was now called "Solution of Arsenic and Mercury" and expressing a desire to have its products accepted for inclusion in New and Nonofficial Remedies. In view of this letter, the committee's report on "Arseno-Meth-Hyd" and the Council's protest against promiscuous intravenous therapy were sent the New York Intravenous Laboratory for consideration.

The reply of the New York Intravenous Laboratory contained nothing which permitted a revision of the preceding report. The change of the name of "Arseno-Meth-Hyd" to "Solution of Arsenic and Mercury" means little as the name still does not disclose the important fact that the arsenic is present as sodium cacodylate, nor does it tell the character of the mercury compound. The Council voted that "Solution of Arsenic and Mercury" and "Arsenoven S. S." be declared inadmissible to New and Nonofficial Remedies because the therapeutic claims advanced for them are unwarranted (Rule 6) and because the names of these pharmaceutical preparations are not descriptive of their composition (Rule 8).

In filing its reply with the Council, the New York Intravenous Laboratory announced that that document would be circulated to the medical profession. This is of course the firm's privilege. The Council notes, however, with interest, that the reply is devoted almost entirely to points which were not raised by the Council and that it fails to discuss the objections which were actually made.

The reply constantly confuses the efficiency of cacodylate in anemia and in syphilis. The Council's report on "Arseno-Meth-Hyd" does not discuss or even touch on the question of cacodylates in anemia. It is confined to a discussion of the disappointing results obtained with cacodylates as such (i. e., without mercury) in the treatment of syphilis. This attempt on the part of the New York Intravenous Laboratory to confuse the issue and to attribute to the Council an opinion that it has never stated or held is an inexcusable misrepresentation. The company in its reply said:

> "We believe that you have previously stated that a solution cacodylate of soda possesses no more action than so much water. In other words, it was inert. Now you try to show that it produces renal injury."

The Council has never declared that cacodylates are inert. In the report it is merely stated "that doses so large as to produce renal injury were almost totally ineffective against syphilis." Neither has the Council stated that cacodylate is "peculiarly dangerous." In fact the absolute toxicity of cacodylates is low but Cole's results were quoted as a caution that "effective" doses are not harmless. A great portion of the remainder of the reply is devoted to disparaging arsphenamin—a product that is not involved in this action of the Council, and one about which the physician is amply informed.

Amongst other wholly extraneous matters, the firm's "reply" tried to resurrect the pepsin pancreatin controversy. This also has nothing to do with the efficiency or harmlessness of sodium cacodylate. In order to dispose of the matter, however, it may be pointed out that the implications are entirely misleading. The work which is quoted against the Council was undertaken by the Council itself, to clarify obscurities in the older data. The outcome of these new investigations showed the essential correctness of the deductions from the older work, namely, that pancreatin is destroyed by pepsin-hydrochloric acid. Dr. Long's work to which the firm's reply evidently refers, showed that under favorable conditions, namely, when protected by an excess of protein, some trypsin may escape destruction in the stomach; but it fully confirmed the original conclusion that

pepsin and pancreatin mixtures as ordinarily administered are practically worthless (J. H. Long, *Jour. Amer. Pharmaco. Assoc.*, Sept. 19, 1917).

As regards the editorial on intravenous therapy, a concession may be made the New York Intravenous Laboratory: intravenous injections are no longer quite as "impressive" as in 1916, but that does not alter the fact that they should be used only when a distinct advantage is to be gained.

HORMOTONE AND HORMOTONE WITHOUT POST-PITUITARY

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Aug. 16, 1919, p. 549

"Hormotone," of the G. W. Carnrick Company, is advertised as "A pluriglandular tonic for asthenic conditions." "Hormotone Without Post-Pituitary" is recommended for use "in neurasthenic conditions associated with high blood pressure." These preparations are sold in the form of tablets for oral administration. The Council declares these preparations inadmissible to New and Nonofficial Remedies because: (1) Their composition is semisecret (Rule 1); (2) the therapeutic claims are unwarranted (Rule 6); (3) they are sold under names not descriptive of their composition but suggestive of indiscriminate use as "tonics" (Rule 8); (4) in the light of our present knowledge the routine administration of polyglandular mixtures is irrational (Rule 10). In explanation of this action, the Council authorized publication of the report which appears below.

W. A. Puckner, Secretary.

Each tablet of "Hormotone" (G. W. Carnrick Co., New York City) is said to contain 1/10 grain of desiccated thyroid and 1/20 grain of entire pituitary, together with the hormones of the ovary and testes—the amounts and the form in which the latter are supposed to be present are not given. From this it will be seen that the only definite information given to the medical profession regarding the composition of Hormotone is that it is a weak thyroid and a still weaker pituitary preparation.

What results can be anticipated from one or two tablets three times daily (the recommended dose of Hormotone) each containing 1/10 grain of thyroid and 1/20 grain entire pituitary? Such doses of thyroid may, of course, have a beneficial action in a limited number of cases of myxedema

and cretinism. An extract of the posterior lobe of the pituitary (Liquor Hypophysis, U. S. P., for example) will, *when injected subcutaneously or intramuscularly,* have a pronounced effect on the parturient uterus; its action on certain other forms of smooth muscle will be much less certain. But the *oral administration* (for which Hormotone is recommended) of the posterior lobe of the pituitary has not been shown to have any such effect. The use of the anterior lobe in doses of 1 to 4 grains (doses very many times larger than those recommended for the entire gland in Hormotone) is in the experimental stage and its only probable value seems to be in those cases of known gland deficiency.

As to the other alleged ingredients of Hormotone—hormones of the ovary and testes, amounts not stated: all physicians know the uncertainties attending the use of ovarian preparations and the serious question as to whether testicular extracts have any therapeutic value. Whatever may be the physician's views as to the probable therapeutic value of these organs, the first thing he desires to know is how much of the substance he is giving and from what part of the gland it is obtained.

So much for the facts; yet the physician is asked to jump from this region of solid fact into a sea of hypothesis; to believe that small amounts of the well-known drugs thyroid and pituitary, plus an unknown amount of unknown hormones of the testes and ovary are of great value in conditions that in themselves are often purely hypothetical. He is asked to believe that this combination has virtues in such conditions as "hypofunction of the adrenal system," neurasthenia, the "fatigue syndrome," amenorrhea, dysmenorrhea, "natural and artificial menopause," sexual neuroses, cold extremities, cardiac asthenia, low blood pressure, infantilism, sterility, melancholic conditions, obesity, anorexia, anemia, slow metabolism, constipation, psychasthenia, lowered virility and the sexual neuroses of the unmarried, hysteria following functional exhaustion of the nerve centers, frigidity, etc., etc., especially if he guesses that the trouble is due to a "pluriglandular disturbance," "glandular hypofunction," an "adreno-pituitary deficiency," suboxidation, etc.

The physician is invited to use Hormotone because, among other reasons, each alleged constituent is said to be "in physiologic sympathy and therapeutic harmony with the others," and further, because:

"Pluriglandular therapy has the endorsement of high authorities, is both logical and effective and Hormotone is a splendid example of it. It will be seen at its best where the patient lacks snap and vim and vigor. Asthenic conditions necessarily indicate hypofunction of the adrenal system . . ." etc.

"The use of gland extracts in the treatment of aplasias of the pluriglandular system has become an established therapeutic measure of miraculous potency (Bayard Holmes: The Internal Secretory Glands, *Lancet-Clinic,* Sept. 19, 1914)."

The G. W. Carnrick Company also advertises a "Hormotone Without Post-Pituitary," each tablet of which is said to contain 1/10 grain desiccated thyroid, and to "present" "hormone bearing extracts of thyroid, anterior pituitary, ovary, and testes." This product is just as irrational as "Hormotone."

FORMALDEHYDE LOZENGES

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Oct. 4, 1919, p. 1077

The Council has voted Hex-Iodin (Daggett and Miller Co., Inc., Providence, R. I.), Formitol Tablets (E. L. Patch Co., Boston), and Cin-U-Form Lozenges (McKesson and Robbins, New York City) inadmissible to New and Nonofficial Remedies, and authorized publication of the report which appears below.

W. A. Puckner, Secretary.

Some years ago, the Council published (The Journal A. M. A., Aug. 28, 1915, p. 816) a report on Formamint, a proprietary medicine widely exploited as a peculiar chemical compound of sugar of milk and formaldehyde. The formaldehyde was said to be liberated slowly by the action of the saliva, and because of this liberation of formaldehyde, Formamint was claimed to be a powerful germicide. Extravagant claims were made for its curative and prophylactic effects. The Council found that the therapeutic claims were grossly unwarranted and that its exploitation to the public was a public danger.

During the recent epidemic of influenza, a variety of tablets or lozenges were advertised, and are still being advertised, having formaldehyde, in some form or other, as the nucleus around which revolve the therapeutic claims. In some cases, the advertising clearly indicates the character of the formaldehyde compound that is claimed to be present; in others the statements are vague and indefinite or misleading.

It is hardly necessary to remind physicians that the use of tablets containing hexamethylenamin or other formaldehyde compounds can neither cure respiratory infections, nor even confer protection against such infections. To be effective, formaldehyde would need to be supplied to the entire respiratory

tract continuously for some time or else in concentrations that would be distinctly irritant and damaging to the tissues. Saliva-dissolved tablets, obviously cannot reach the nasal or tracheal mucosae directly; and the application of quickly acting concentrations of formaldehyde is out of the question. This altogether aside from the fact that hexamethylenamin, the basis of some of these tablets, does not liberate formaldehyde in the mouth, and for this reason alone would be quite useless for this purpose! (See Hanzlik and Collins, *Archives of Internal Medicine,* November, 1913.)

An inefficient antiseptic is more than merely useless; it is a menace to public safety, in that it tends to lead to the neglect of rational and effective protective measures. It therefore seems advisable for the Council again to call the attention of physicians to the subject. Accordingly, three specimens of these products were purchased and examined in the Association's Chemical Laboratory.

Hex-Iodin

Hex-Iodin (Hexamethylenetetramine and Iodum) Lozenges are manufactured by Daggett and Miller Company, Inc., Providence, R. I. They weigh 15½ grs. each, are sweetened and are flavored with mint or menthol. The package and circulars do not contain a definite statement of composition. The rather indefinite synonyms "Hexameth. and Iodine Comp." and "Hexamethylentetramine and Iodum" suggest that the lozenges contain hexamethylenamin and free iodin. The further statement that they "contain the combined medicinal antiseptic and prophylactic properties of Hexamethylenetetramine and Iodum" is also rather indefinite. The therapeutic action claimed for the lozenges, however, could only be produced by free iodin and by liberated formaldehyde.

It is unnecessary to discuss in detail the extravagant claims made for these lozenges. The inefficiency of hexamethylenamin has already been referred to; the limitations of iodin, free or combined, in lozenge form, need not be discussed because the examination made in the A. M. A. Chemical Laboratory showed that Hex-Iodin lozenges contained no free iodin, and only traces of combined iodin. Neither formaldehyde nor paraformaldehyde was present; hexamethylenamin was present but, the lozenges being neutral no formaldehyde is generated in contact with water or with the alkaline saliva.

Thus Hex-Iodin is shown to be worthless for the purpose for which it is advertised. Of the two important ingredients

said to be present, iodin and hexamethylenamin, only traces could be found of the former while the latter, as has been shown, is incapable of exerting any effect when used as the manufacturers direct.

Formitol Tablets

These tablets are prepared by the E. L. Patch Co., Boston. Each tablet weighs 13½ grs. They have the odor of thymol or menthol and an acid taste and reaction. They are, according to the label:

"For the throat and mouth. Soothing, Astringent, Antiseptic. Rapidly destroys germs of infection, preventing and relieving sore throat and mouth."

In a circular, it is stated, that one of the qualities of Formitol:

". . . is the generation of formaldehyde when in contact with water or the saliva."

"Besides generating formaldehyde, Formitol, Patch contains astringent, demulcent and soothing ingredients which render the combination unusually effective."

A bacteriologic report is given in this circular in which it is stated that, in 2½ minutes one Formitol Tablet rendered sterile a plate culture of a "characteristic throat micrococci." The instructions are to dissolve a tablet in the mouth, slowly, once an hour or a half-tablet every half hour.

The A. M. A. Chemical Laboratory reported that Formitol Tablets contained formaldehyde (or paraformaldehyde), an ammonium compound, and some hexamethylenamin. It is probable that the formaldehyde (or paraformaldehyde) was produced by the decomposition of hexamethylenamin originally present in the tablets but decomposed by long contact with the acid.[1]

These tablets differ from Hex-Iodin in that they really contain active formaldehyde and, therefore, possibly produce antiseptic effect in test-tube cultures. The conditions in the mouth, however, are very different from those in the test-tube, since in the mouth the formaldehyde would be immediately "bound" or absorbed. The claimed absence of irritation indicates sufficiently the absence of efficient quantities of formaldehyde under clinical conditions.

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1. The E. L. Patch Company declares that "no hexamethylenamine has ever been used in the manufacture of Formitol tablets," and that ammonium chloride and paraformaldehyde are among the ingredients used in the manufacture of these tablets. The hexamethylenamine present in the tablets, therefore, must have been produced by interaetion of the paraformaldehyde and ammonium chloride. This does not alter the laboratory findings regarding the composition of the tablets, namely, that they "contain formaldehyde (or paraformaldehyde), an ammonium compound and some hexamethylenamine."

Cin-U-Form Lozenges

Cin-U-Form Lozenges, manufactured by McKesson and Robbins, New York City, are marketed in bottles of 24 for 25 cents. They have a strong odor of cinnamon, weigh 15½ grs. each, and are acid in taste and reaction. The label states that they contain:

"Cinnamon, Eucalyptus, Formaldehyde and Menthol—all powerful germicides against Influenzal bacilli, but not injurious to the system in this palatable form."

A circular contains the same statement as to composition and claims further that they:

". . . help to prevent the infection of Spanish Influenza, Pneumonia, Grip Colds and to guard against Sore Throat, Tonsilitis, Pharyngitis, etc."

The A. M. A. Chemical Laboratory reported that Cin-U-Form Lozenges contained some formaldehyde (or paraformaldehyde) and no hexamethylenamin. It is obvious that the mouth and throat cannot be "disinfected" by these lozenges. They would be totally ineffective against bacteria that enter through the nose; they cannot prevent influenza, pneumonia, etc.

LAVORIS

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Nov. 1, 1919, p. 1380

Lavoris was considered by the Council in 1913, and its proprietors—the Lavoris Chemical Company—were advised that the preparation was inadmissible to New and Nonofficial Remedies because of conflict with Rules 1, 4, 6, 8 and 10. No report was published at that time. As the preparation is still widely advertised to physicians, the Council has again examined Lavoris and authorized publication of the following report. W. A. PUCKNER, Secretary.

In recent years Lavoris has been widely advertised as "THE IDEAL ORAL ANTISEPTIC," particularly to the dental profession. A printed card sent out by the Lavoris Chemical Company in 1913 read: "LAVORIS, the Pyorrhea Remedy. The Original ZINC CHLORIDE Mouth Wash. One grain zinc to each ounce." The card also gave a "formula" to the effect that each pint of Lavoris contained:

Zinc Chloride	1.040
Resorcin	0.520
Menthol	0.400
Saccharin	0.195
Formalin	0.195
Ol. Cassia Zeyl	0.780
Ol. Caryophyl	0.195

Advertisements now appearing in medical journals repeat the older "formula" except that resorcin is omitted. The formula while seemingly frank and open is in reality indefinite and misleading in that no denomination of weight is given for the various constituents. It is uncertain, for example, if the figures in the formula are intended to represent grains, grams or percentages of the several constituents. In view of the indefinite statement of composition, a chemical examination of Lavoris was undertaken in the A. M. A. Chemical Laboratory. The report of the laboratory follows:

Zinc.—This was determined electrolytically. Fifty c.c. gave 0.026 gm. zinc and 100 c.c. gave 0.0531 gm. zinc. The average is 0.0526 gm. zinc in 100 c.c. This is equivalent to 0.1102 gm. anhydrous zinc chlorid in 100 c.c.

Chlorid.—After decolorizing some of Lavoris with chlorid-free animal charcoal, the chlorid was determined by the Volhard method. Twenty-five c.c. Lavoris required 4.328 c.c. tenth-normal silver nitrate solution equivalent to 0.01535 gm. chlorid (chloridion) or 0.0614 gm. in 100 c.c. A second 25 c.c. of Lavoris required 4.112 gm. tenth-normal silver nitrate solution equivalent to 0.01458 gm. chlorid (chloridion) or 0.05832 gm. in 100 c.c. Average is 0.05985 gm. This is equivalent to 0.1150 gm. zinc chlorid in 100 c.c. This agrees closely with the foregoing zinc determination.

Resorcin.—The method of the U. S. Pharmacopeia was used. The total bromin absorption of 25 c.c. Lavoris was 3.68 c.c. tenth-normal bromin solution. This would be equivalent to 0.00675 gm. resorcin in 25 c.c. or 0.02700 gm. in 100 c.c. In a duplicate test, 25 c.c. Lavoris required 3.8 c.c. tenth-normal bromin solution equivalent to 0.00697 gm. resorcin or 0.02788 gm. in 100 c.c. Since oil of cinnamon absorbs bromin, 50 c.c. of Lavoris was boiled until very little or no odor of the oil was noted, keeping the volume nearly constant by adding a little water from time to time, and the bromin absorption then taken. In one experiment, 0.36 c.c. of tenth-normal bromin solution was consumed, and in a duplicate no bromin was absorbed. This shows the absence of resorcin.

Residue.—On evaporating 25 c.c. Lavoris on a steam bath and subsequent drying of the residue at 100 C., 0.0455 gm. of residue was obtained. This is equivalent to 0.1820 gm. in 100 c.c.

Saccharin.—Saccharin was detected in the residue and ether-extract of the residue by its intense sweet taste when a little sodium bicarbonate was added to it.

Formaldehyd.—This could be detected by the Jarrison test. The color was not very pronounced and the quantity of formaldehyd was small.

Oil of Cinnamon.—The odor and taste of Lavoris is characteristic of cinnamon.

Menthol and Oil of Cloves.—The odor of menthol and of oil of cloves could not be detected, but no tests were made to demonstrate their presence.

The analysis thus indicates that the Lavoris of today contains no resorcin but does contain a small amount of formaldehyd, a little saccharin, and oil of cinnamon (menthol and oil of cloves could not be detected by the odor, but were not tested for). The analysis showed that the principal constituent of Lavoris is zinc chlorid, of which there is about 0.1 gm. per 100 c.c. (about ½ grain to the ounce).

The amount of zinc chlorid given in the published formula, i. e., 1.04, is meaningless because the unit of weight or measure is not given; furthermore the analysis shows that it is inaccurate for any unit of weight that might be assumed from the published figures. Since the amount of the most active medicinal ingredient is both indefinite and inaccurate, the composition of the preparation is essentially secret. Lavoris is indirectly advertised to the public by having included in the package a circular giving a list of diseases for which the preparation was recommended. The combination of zinc chlorid, formaldehyd and oil of cinnamon (assuming the menthol and oil of cloves to be present as flavors) in a mixture is irrational and likely to lead its users to ascribe a false and exaggerated value to the preparation. The name is objectionable in that it does not indicate the composition of the potent ingredients of the mixture, but instead suggests its use as a mouth wash.

From a standpoint of public safety, the most serious objection to Lavoris, however, lies in the many unwarranted therapeutic claims and suggestions. It is generally held that zinc chlorid solutions which possess a strength of from 1 to 200 up to 1 to 500 exercise a weak antiseptic action. The strength of zinc chlorid in Lavoris is approximately 1 to 1,000. The directions for its use recommend that Lavoris should be diluted. A dilution of 1 to 4 is recommended for a variety of mouth conditions while for cystitis irrigations and as a vaginal douche, it is recommended that one tablespoonful be added to a quart of warm water or salt solution. The strength of zinc chlorid in the last suggested dilution would approximate 1 to 64,000. It is evident that no antiseptic action could be expected from such dilutions.

The recommendation that diluted Lavoris be used for the treatment of coryza, nasal catarrh, hay fever, inflamed eyes, hemorrhoids and leucorrhea is objectionable and irrational.

Especially dangerous is the recommendation that members of a family exposed to diphtheria or scarlet fever should use Lavoris freely as a preventive. Such recommendations can but give a false sense of security and lead to the neglect of proved methods for preventing the spread of these diseases. Equally unwarranted is the recommendation that in gonorrhea one teaspoonful of Lavoris to eight of warm water be used with a blunt end syringe.

The use of Lavoris as recommended would not only prove valueless in many instances but might lead to serious consequences because really valuable methods of prevention or treatment might be neglected. For these reasons the preparation is in conflict with Rule 6.

The Council declared Lavoris ineligible for New and Nonofficial Remedies.

ACRIFLAVINE AND PROFLAVINE, N. N. R.

Conclusions to Be Drawn from a Study of the Literature

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Nov. 15, 1919, p. 1542

Acriflavine and proflavine have been accepted for New and Nonofficial Remedies. A description of these drugs, with a discussion of the uses and dosage and tests of identity and purity was published in the New and Nonofficial Remedies Department of THE JOURNAL, Nov. 8, 1919, page 1443. The following report briefly summarizes the literature at present available on these drugs.

W. A. PUCKNER, Secretary.

It has been known for some time that certain dyes possess bactericidal and amebicidal properties, while others have no effect as antiseptics or germicides. After this discovery was made, chemical research was begun in the effort to produce substances which should have higher bactericidal potencies than those already known. In these studies it was found that certain of the acridine derivatives were especially active as amebicides. Acridine is a substance first obtained from coal-tar. Some of its derivatives have been known and used as dyes for many years, certain of them being known as flavines because of the yellow color they impart to fabrics.

Most of the acridine derivatives have no amebicidal properties; but, as already stated, there are some marked exceptions. One of these (diamino-methyl acridine chloride) was found by Ehrlich to have notable therapeutic effects in trypanosome infections and, on this account, he called it "Trypaflavine." Most of the studies on this substance, both

bacteriologic and clinical, have been conducted by English investigators, who call it "Acriflavine." A closely related substance having similar properties is "Proflavine." Acriflavine and proflavine are claimed by some to have high antiseptic power, together with freedom from toxic or irritant action and without inhibiting effects on the phagocytic action of the leukocytes or on the healing processes. Acriflavine and proflavine have been extensively used in the treatment of wounds, and acriflavine has been highly praised in the treatment of gonorrhea.

In view of the interest manifested in the therapeutic properties of acriflavine and related compounds, as evidenced by numerous inquiries from physicians to the Council on Pharmacy and Chemistry, the Council has deemed it worth while to prepare and publish an abstract of the available literature on the subject. Tentative descriptions and standards for acriflavine and proflavine are published in New and Nonofficial Remedies for the information of manufacturers, pharmacists and physicians.

It should be borne in mind that the therapy of these dyes is still in the experimental stage. The evidence at present available does not permit a determination of their value in the treatment of wounds, trench fever, or gonorrhea. A number of papers have been omitted purposely from this abstract of the literature because they presented no additional contribution to the knowledge of the dyes or their therapeutic properties.

ABSTRACTS OF THE LITERATURE ON ACRIFLAVINE AND PROFLAVINE

Benda[1] described the preparation and properties of 3:6 diamino acridine and of 3:6 diamino-10-methyl acridinium chlorid. The first named substance is now known as proflavine base, its sulphate being called "Proflavine." The methyl acridine compound is now called "Acriflavine." The word "flavine" in the literature usually refers to "Acriflavine," but its use in this connection is discouraged because of confusion with the vegetable dye, flavine.

Browning and Gilmour[2] by bacteriologic technic found that diamino acridine is a more powerful bactericide than acridine yellow.

After a bacteriologic examination of a number of antiseptics, supplemented by more than 2,000 clinical tests with some of the substances, Browning and others[3] conclude that flavine (acriflavine) possesses the highest sum of desirable properties for therapeutic purposes of any antiseptic. It is claimed to have high antiseptic power, together with freedom from toxic or irritant action and without inhibiting effects

on the phagocytic action of the leukocytes or on the healing processes. Flavine is more efficient and more rapid than brilliant green.

Ligat[4] treated upward of 150 septic cases, 50 per cent. of which were war wounds, with brilliant green and flavine compounds. Controls using other antiseptics were not carried out. He finds flavine to be more efficient than the green dye. He regards these substances as satisfying therapeutic requirements for the treatment of wounds in a manner superior to any of the antiseptics hitherto employed. Adequate drainage by free incision is first secured, and the wound then irrigated, 1:1,000 in physiologic sodium chlorid solution.

After a considerable number of clinical trials, fifty-five of which were war wounds, James[5] considers that flavine constitutes an exceedingly valuable addition to the armamentarium of the surgeon in the treatment of septic wounds, and as a therapeutic agent, is much superior to any other substance, including hydrogen peroxid and chlorinated compounds, with which he had experience. Flavine leads much more rapidly to the extinction of infection, as evidenced by the disappearance of suppuration.

Gray[6] reports that the use of flavine as an intraspinal injection in cerebrospinal fever has been distinctly unfavorable.

Wells[7] found that a solution containing sodium desoxyocholate, 2 per cent., quinin hydrochlorid, 0.25 per cent., and flavine, 0.05 per cent., used as a mouth-wash, gave the best bactericidal effects on the pneumococcal strains of the mouth. Even after four hours, the bacterial count was less than the control.

Bond[8] discusses the use of acriflavine soap paste, acriflavine gelatin and acriflavine starch mucilage as dressings for infected wounds. For continuous application, a 1:2,000 aqueous solution is better than stronger solutions.

Browning and others[9] find that flavine compounds and brilliant green are antiseptics which exert a slowly progressive bactericidal action. Flavine compounds are enhanced in bactericidal potency by serum; brilliant green is reduced in activity by serum. For this reason, in the opinion of these investigators, the flavines are preferable to brilliant green in the treatment of wounds. The bacteriologic tests were carried out on *Bacillus coli* and on *Stahpylococcus aureus* with controls. Comparisons were made with chloramin-T, mercuric chlorid and phenol. The bactericidal effects of the flavine dyes are slower to appear than are the effects of the other antiseptics tried, but the ultimate results are much greater.

Fleming[10] reports that flavine has a marked destructive action on the leukocytes, the effects being more pronounced than on bacteria in a twenty-four-hour test. A 1:100 solution injected into the pleural cavity loses its bactericidal

power in twenty-four hours. In pus, phenol has a bactericidal coefficient 250 times that of flavine in twenty-four-hour tests. These findings are at extreme variance with those of Browning and others, as reported above.

Hewlett[11] finds by bacteriologic tests that the germicidal value of flavine is much lower than had been reported by Browning and his co-workers. Hewlett employed much larger numbers of organisms in the tests than did Browning and others, which may account for the difference in results. The findings agree in a general way with those of Fleming.

Drummond and McNee[12] treated seventy patients (120 wounds) with flavine in 1:1,000 solution and 1:5,000 solution. The advantages of the antiseptic appear to be: (*a*) There is absence of toxicity; (*b*) suppuration and the spreading of sepsis are prevented; (*c*) the primary dressings need not be changed for two or three days, after which they are painlessly removed, and (*d*) the wounds are not inflamed or painful. Excision of the damaged tissue and cleaning of the wound are necessary preliminaries. The 1:1,000 solution is recommended for the primary dressing, and the 1:5,000 solution for later dressings. Flavine is not recommended in the treatment of the later stages of wounds. Controls using other antiseptics were not carried out.

College, Drummond and others[13] report that in a series of sixty recent war wounds (forty-seven patients) treated with proflavine, there appeared to be no difference between the results obtained with proflavine and those from acriflavine previously reported (see preceding abstract). Controls with other antiseptics were not carried out. Proflavine is more easily produced than acriflavine.

Browning and Ligat,[14] in a review of the status of wound treatment with flavine compounds, conclude "that the most valuable effects of flavine antiseptics are to be obtained in the first few days of application, and that later on, after serious infective processes have been prevented or overcome, it is advisable to intermit their use or to substitute some other compound—thus, to prevent the appearance of sepsis and to control it when established are results which flavine antiseptics undoubtedly have shown themselves capable of accomplishing with a very great measure of success, by comparatively simple procedures."

Carslaw[15] used acriflavine in twenty-two infected war wounds with uniformly satisfactory results. He concludes that lacerated, infected wounds respond much more rapidly to flavine treatment than to other antiseptics. After four or five days he advises discontinuance of the flavine dressings and the use of some other antiseptic.

Bryan and others[16] used acriflavine (1:1,000 in physiologic sodium chlorid solution) intravenously in trench fever. Good results in six cases out of seven were reported. Treatment in the seventh was incomplete. "Galyl" was considered inferior.

Dakin and Dunham,[17] from the results of comparative bacteriologic tests, believe that the statements of Browning and his coleagues as to the relative germicidial efficiency of chloramin-T and other antiseptics of the chlorin group compared with brilliant green, malachite green, and acriflavine, are incorrect, and that their mode of testing the germicidal action of the substances studied by them leads to conclusions which are radically misleading.

Bashford and others[18] report on a study of fifty cases of war wounds treated with flavine, as compared with fifty similar but more severely wounded cases treated by the Carrel-Dakin system. The investigation showed that a solution of 1:1,000 of acriflavine, far from being innocuous, produces very deleterious effects on the entire process of healing, killing successive layers of the reacting tissue elements, including the essential vascular mechanism. The flavine treatment of wounds is associated with but slight formation of pus, slow epithelial ingrowth, delay in all the processes of repair, lingering of organisms on the wound surface, and some diminution in the local and general reaction to infection. The only favorable feature has been that the patient is apparently protected in some way from the absorption of toxic products.

Hillyer[19] treated a knee joint, which had been repeatedly aspirated without healing, by injections of flavine solution (1:1,000). Healing began at once and progressed to favorable termination.

Pilcher and Hull[20] have treated over 5,000 cases of wounds with flavine. They report that for ease of preparation and application, rapidity when dealing with large numbers of cases, complete absence of surgical fidget, early cleansing of the wounds, and abatement of constitutional reaction to absorption, flavine is an admirable application under all circumstances, but especially when surgeons are few, time is short, and wounds are many.

From bacteriologic studies, Morgan[21] found that acriflavine is more potent than proflavine in antiseptic and toxic properties. It has a very marked inhibiting effect on streptococci and a less marked action on staphylococci. On some organisms its effects are insignificant. It has a marked but slow toxic action on tissues, but not so great as to prohibit its use in 1:4,000 solution as a dressing for wounds infected with streptococci or staphylococci.

Pearson[22] used flavine, 1:1,000, in physiologic sodium chlorid solution in wound treatment. In cases in which infection and sepsis were active and uncontrolled, the use of flavine following suitable operative treatment had no beneficial effect on the subsequent progress of the case, so far as control of sepsis was concerned. Any slight differences observed were unfavorable. In cases in which sepsis had already been controlled and repair had begun, flavine acted

injuriously, chiefly by producing an unhealthy granulating surface. Pearson thinks the clinical use of flavine is not attended with good results. No bacteriologic control tests were made.

Carslaw and Templeton[23] investigated acriflavine and proflavine as therapeutic measures in the treatment of gunshot wounds with the view of ascertaining which was the better. Although the action of the substances is similar, there can be no doubt that the action of proflavine is slower. These salts are of undoubted value in controlling and preventing the spread of sepsis, as is shown by the rapid improvement in local and general conditions. There is no evidence of any general toxic effect. The application of flavine does not render an infected wound sterile in the bacteriologic sense. In twenty-seven out of sixty cases the clinical obervations were supplemented by bacteriologic tests.

Davis and Harrell[24] found that acriflavine inhibits the development of the gonococcus in protein-containing mediums, in dilution of 1:300,000. It is nontoxic and but slightly irritant to the urethral mucous membrane. The average duration of a gonorrhea is distinctly lessened under treatment with acriflavine. In an occasional case the dye had no effect, while in many cases it acted almost as a specific. Recurrences were noted as in other forms of treatment.

Davis and White,[25] from preliminary experiments made on rabbits and dogs, conclude that acriflavine and proflavine may prove of value for internal use in alkaline infections of the urinary tract.

Savery[26] indorses the use of flavine in septic injuries. All affected parts should be reached by the antiseptic, introduction of the solution by a hypodermic syringe being resorted to if necessary. The flavine soaked gauze should be applied as wet as possible. Flavine gives best results by intermittent use with other antiseptics, such as hypochlorites, brilliant green or magnesium sulphate. This method has given great satisfaction.

Berkeley and Bonney[27] have used an ointment of proflavine oleate 1 part, and paraffin and calcium carbonate 49½ parts each, with success as a wound dressing in injuries in which there were exceedingly tender raw surfaces, the dressing of which caused acute pain. The dressing does not dry like aqueous antiseptics, and when removed it strips off from the sensitive surfaces without any dragging or pain. The initial dressings need not be changed for several days.

Tubby and others[28] used an acriflavine paste in the treatment of wounds, and acriflavine in solution also. The paste was composed of bismuth subcarbonate, 25 per cent., paraffin, 75 per cent., and acriflavine, 0.5 per cent. This paste was used in place of bismuth iodoform paraffin paste and, it is believed, with better results. Gauze soaked in acriflavine solution and applied to wounds as a dressing had no advantage over hypochlorites. Under acriflavine solution treat-

ment, granulations often become sluggish and indolent. The authors were not able to see that acriflavine solution was superior to all others yet introduced in combating bacterial growth in wounds or in promoting rapid healing. They consider that the solution is far less useful than the paste.

Stowell[29] has had good results from the use of a sterile emulsion consisting of acriflavine, 0.1; thymol, 0.005; white wax, 4.0; liquid petroleum, 76, and water, 20. He has been disappointed in the results obtained from acriflavine, 1:1,000, in physiologic sodium chlorid solution.

Browning and Gulbransen[30] review the bacteriologic investigations on the flavines and report further experimental work. Extended investigations confirm the original values found for the antiseptic and bactericidal preparations, acriflavine, proflavine and brilliant green. Inferior potencies reported by other workers are considered to be due to faulty technic, which failed to detect bacteriostatic action, i. e., inhibition of bacterial activity, which is a marked property of these compounds. The flavines, in view of their low toxicity to mammalian tissues and high bacteriostatic power, are well suited to act as local therapeutic agents. Since they are not neutralized by serum, they do not require frequent renewals in wounds.

Gibson[31] believes that the best antiseptic for irrigation in gonorrhea is flavine solution in strengths of from 1:6,000 to 1:8,000. He treated thirty-seven cases with hydrogen peroxid injections followed by irrigation with potassium permanganate. The average length of treatment was 105 days. The results were unsatisfactory. Irrigation with Wright's hypertonic saline, followed by injections of protargol, was used in seventy-one cases for an average of ninety-four days. The treatment was a failure. In twenty cases treated successfully with flavine, the average length of treatment was forty-eight days. Some of the patients in each group received vaccines.

Watson[32] concludes that lavation with acriflavine solution (1:4,000) is the most satisfactory routine treatment for acute gonorrhea at present available.

As a result of an extended series of microbiologic tests on cats and rabbits and on the blood corpuscles of sheep and rabbits, Tubby and others[33] conclude that no definite curative influence can be demonstrated either with proflavine or with acriflavine in the treatment of bacillemia due to organisms injected. This is only what might be expected in view of the rapidity (as shown by the experiments) with which the flavines are eliminated from the circulation. If the intravenous injections of flavine solutions be made very slowly, the agglutinating effect is reduced to a minimum. Proflavine is about half as toxic to rabbits as acriflavine.

Armstrong[34] reports unfavorable results from the use of acriflavine in twenty-three cases of uncomplicated gonorrhea.

SUMMARY

A review of the literature abstracted shows that of the thirty-four reports twenty-five, or 73 per cent., may be considered as favorable. Seven, or 20 per cent., are distinctly unfavorable, and two, or 7 per cent., are in the negative or doubtful class. Of the favorable reports, eight are based for the most part on bacteriologic studies or are of a discursive nature, fourteen are based principally on clinical trials, and three appear to be deduced from a combination of bacteriologic and clinical methods. Of the unfavorable and doubtful reports, five are based on bacteriologic studies and four on clinical trials. Because of the contradictory nature of the reports and the conflicts in the clinical evidence, it would appear that judgment as to the therapeutic value of the flavine dyes should be suspended pending further study.

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MEDINAL

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Nov. 15, 1919, p. 1543

The Council has authorized publication of the following report on Medinal (Schering and Glatz, Inc.).

W. A. Puckner, Secretary.

Medinal is a proprietary name applied to barbital sodium (sodium diethylbarbiturate) the sodium salt of barbital (diethylbarbituric acid). The latter was first introduced as Veronal.

Medinal was deleted from New and Nonofficial Remedies in 1916 because the advertising issued by Schering and Glatz (who then acted as agents for Chemische Fabrik auf Actien vorm. E. Schering, the German manufacturer) contained misleading and unwarranted therapeutic claims. The Council did not publish its report because by the time the report

was ready for publication the product was practically off the American market, and it was hoped that when Medinal again became available, Schering and Glatz would revise the claims and thus permit its reacceptance.

Medinal, said to be manufactured in the United States, is now marketed by Schering and Glatz, Inc. In October, 1918, the firm sent to the Council a typewritten copy of a proposed circular for Medinal. The firm was informed that this leaflet was subject to the objections that had been raised when Medinal was deleted from New and Nonofficial Remedies. In April, 1919, the firm submitted a printed circular which it was sending out. This contained numerous misleading statements, among them, these:

"MEDINAL removes its [Diethylbarbituric acid] one objectionable feature—insufficient solubility—and thus fulfills the three prerequisites of a truly rational hypnotic: Quick absorption, insuring prompt action, rapid and complete excretion, affording protection from cumulative toxic after effects, and the choice of rectal and subcutaneous administration."

There is no justification for the claim that diethylbarbituric acid (barbital) has only one objectionable feature and that a minor matter of "insufficient solubility." The Council has called the attention of Schering and Glatz, Inc., to the fact that the difference in the time of absorption between Medinal (barbital sodium) and barbital is, at the most, but one of minutes and that there is no evidence that Medinal is excreted more rapidly than barbital. Hence the claims that the danger of toxic side-actions and that cumulative after-effects are avoided in this product, are wholly unwarranted.

It is also claimed, and the claim is unsupported by satisfactory evidence, that Medinal is useful in the insomnia of tuberculosis in which condition it is said to have a double advantage owing to its favorable effects on the night-sweats. It is claimed that Medinal is used in the withdrawal treatment of morphin addiction with great success; there is no evidence that Medinal has any special usefulness in this treatment of the morphin habit. It is claimed further that success has been reported with Medinal in the treatment of whooping cough. The Council knows of no satisfactory evidence to show that Medinal is of special value in whooping cough; on the contrary, it is capable of doing a great deal of harm. The recommendations that Medinal be used for the control of labor pains and in acute neuralgic pains that resist other forms of treatment are wholly unwarranted as the value of the drug in such conditions is inherently improbable and until satisfactory evidence in support of them is forthcoming, must be deemed misleading.

OMISSION OF COTARNIN SALTS (STYPTICIN AND STYPTOL) FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Nov. 22, 1919, p. 1628

The Council has authorized publication of the following report. W. A. PUCKNER, Secretary.

Salts of the base cotarnin have been used as local and systemic hemostatics. The hydrochlorid was first introduced as "Stypticin," and is now in the pharmacopeia as cotarnin hydrochlorid (*Cotarninae Hydrochloridum, U. S. P.*). The phthallic acid salt of cotarnin—cotarnin phthallate—was introduced as "Styptol." Both Stypticin and Styptol were admitted to New and Nonofficial Remedies. In 1918 the Council voted to omit Stypticin because the former American agents were no longer offering it for sale. Styptol was retained and is described in N. N. R., 1919.

As was pointed out in the description (N. N. R., 1918), the evidence for the usefulness of the cotarnin salts has been contradictory and unsatisfactory; but since the available data against the efficiency were at least equally unreliable, the Council deemed it best to retain them in N. N. R. pending a thorough investigation of the subject. This was undertaken by P. J. Hanzlik, at the suggestion of the Therapeutic Research Committee of the Council.

A reliable judgment of hemostatic efficiency can be formed only on a basis of strictly controlled conditions, which can best be furnished in the laboratory. Hanzlik repeated the principal experiments published by previous investigators, and applied a number of new or improved methods. The results (published in the *Journal of Pharmacology and Experimental Therapeutics* **10**:523, 1918; **12**:71, 1919) show the following:

Direct Application to Wounds.—The widely quoted results of the gynecologist K. Abel, on the footpad of cats, were found to be quite unreliable. When the experiment is properly controlled, the results are either negative or the bleeding may be increased. Quantitative experiments on wounds of the footpad of dogs showed that cotarnin invariably *increased* the bleeding. Equally negative or unfavorable results were obtained with wounds to the comb of roosters, and to the liver and spleen.

Direct Action on Vessels.—The results of perfusion experiments were variable, but, in general, showed a vasodilation action instead of constriction. This holds true also of the

uterine vessels. The vessels in the living animal (rabbit's ear) were also unaffected.

Systemic Administration.—The bleeding from an irrigated wound was not modified directly by intravenous injection of cotarnin salts, but varied merely with the state of the blood pressure.

The evidence for the inefficiency of cotarnin salts as hemostatics seemed so conclusive as to warrant the Council in rescinding the acceptance of Styptol, and directing the omission of the general article on cotarnin salts and the description of Styptol from New and Nonofficial Remedies.

MICAJAH'S WAFERS AND MICAJAH'S SUPPOSITORIES

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Nov. 29, 1919, p. 1715

"Micajah's Medicated Wafers" and "Micajah's Suppositories," sold by Micajah & Co., Warren, Pa., are declared inadmissible to "New and Nonofficial Remedies" because (1) their composition is essentially secret (Rule 1); (2) the name of neither of these mixtures is indicative of its composition (Rule 8); (3) of exaggerated and unwarranted therapeutic claims (Rule 6), and (4) the therapeutic advice which accompanies the trade packages constitutes an indirect advertisement to the public (Rule 4).

W. A. Puckner, Secretary.

Micajah's Medicated Wafers (formerly called "Micajah's Medicated Uterine Wafers") were analyzed in the A. M. A. Chemical Laboratory in 1910. They were found to consist essentially of dried ("burnt") alum, boric acid and borax, in approximately the following proportions:

Alum, dried	59.86 per cent.
Borax, dried	15.62 per cent.
Boric acid	5.67 per cent.
Water of hydration	18.85 per cent.

There are a number of drugs that are more or less effective in the treatment of local lesions of mucous membranes and the skin. They are classed as astringents. Among these are included alum, borax and boric acid. Every physician has used them. To say that a wafer consists of alum, borax and boric acid inspires but little awe. But there is something much more mysterious and impressive in declaring that a wafer "consists of an astringent and antiseptic base,

in which are incorporated certain medicaments which both locally and after absorption, contribute to the astringent, antiphlogistic, depletive, soothing and healing action of the product." This gives the impression that some powerful and almost incomprehensible factors are at work. Yet, after all is said and done, the substances contained in Micajah's Medicated Wafers are just the homely old alum, boric acid and borax.

In addition to "Micajah's Medicated Wafers," Micajah & Co. also put out "Micajah's Suppositories for Hemorrhoids." These have been examined in the A. M. A. Chemical Laboratory and, like the "Medicated Wafers" have been found to contain alum, boric acid and borax—and these substances practically alone—incorporated in cocoa butter. The company claims that "to these have been added Ammonii Ichthyosulphonate, Balsam of Peru, Ext. Belladonae." The A. M. A. chemists report, however, that if extract of belladonna is present at all it is in amounts too small to be detected by the method commonly employed in the chemical examination of alkaloidal drugs. The chemists report further that while ammonium ichthyosulphonate and balsam of Peru both have a decided odor and are dark in color, the suppositories have but little color and the odor of the cocoa butter that forms their base is not covered by these drugs; obviously, therefore, if ammonium ichthyosulphonate and balsam of Peru are present at all it is in amounts utterly insufficient to exert any therapeutic effect.

It would be hard to find better examples of michievous proprietary medicines than these two products of the Micajah Company. "Twins of Efficiency," they are called in an advertising pamphlet. The composition is not stated. A physician using the "twins" does so absolutely in the dark. To him they are secret preparations. He is encouraged to use them in a great variety of conditions in which other drugs are much more useful. Inevitably, physicians using them will be likely to overlook, or pass over, new growths, specific infections and diseases that require radical remedial measures.

In addition to misleading and exaggerated claims, there is a reference to a report from the usual "well-known and reliable bacteriological laboratory." The excepts published from this report of an unnamed laboratory are sufficiently vague to incriminate no one.

From time to time it is worth while to emphasize facts regarding proprietary medicines that while obvious are sometimes forgotten. For this reason attention is directed to Micajah's Uterine Wafers and Micajah's Suppositories.

LACTIC ACID FERMENTS

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Dec. 20, 1919, p. 1895

The following report has been authorized for publication by the Council. The revised general article on Lactic Acid-Producing Organisms and Preparations, which will appear in New and Nonofficial Remedies, 1920, is published in the New and Nonofficial Remedies department of this issue of THE JOURNAL.

W. A. PUCKNER, Secretary.

In preparing the 1920 edition of New and Nonofficial Remedies it seemed desirable to give careful reconsideration to the use, in medicine, of lactic acid bacteria—and products prepared by means of these bacteria—in relation to practical therapy. A special committee consisting of a physiologic chemist (Lafayette B. Mendel, chairman), a pediatrist (John Howland), an internist (W. P. Longcope), a rhinologist (H. I. Lillie) and a bacteriologist (L. F. Rettger) took up the problem. The following circular letter was sent to a large number of well-known bacteriologists, clinicians and manufacturers who might be assumed to have experience or information which would enable them to express a helpful opinion on certain debated questions relating to the practical use of lactic acid bacilli in clinical medicine:

> "*Dear Doctor:* The Council has been discussing the question as to whether or not the lactic acid-producing organisms, and preparations produced by their action, shall be retained in New and Nonofficial Remedies; and if so, what, if any, revision should be made of the general discussion now appearing in the book.
>
> "Although there is still wide diversity of opinion as regards the possible value of these products, either as administered by mouth or for application to arrest putrefaction in wounds, the enthusiastic support of their use on the part of their former advocates seems to have abated in recent years. As the time for more exact judgment concerning their therapeutic value appears opportune, the Council would value your opinion on any or all of the following questions:
>
> "1. Do you regard the administration of milk soured by means of the Bulgarian bacillus, alone or in combination with other organisms, to have advantages over the administration of sweet milk, buttermilk or milk soured in the ordinary way? If so, what advantages may properly be ascribed to milk preparations obtained by action of the Bulgarian bacillus?

"2. Do you consider it rational to administer preparations containing viable cultures of the Bulgarian bacillus with the expectation of securing their implantation in the intestinal canal? On what facts or evidence do you base your opinion?

"3. Do you consider the application of cultures of the Bulgarian bacillus to infected suppurating sinuses, cavities, etc., rational? On what facts or evidence do you base your opinion?

"4. If in your opinion there is therapeutic value in products of Bulgarian bacilli, what revision of the article 'Lactic Acid-Producing Organisms and Preparations' which now appears in New and Nonofficial Remedies (see enclosure) would you advise?

"5. Have you had occasion to employ preparations of viable cultures of *Bacillus acidophilus* for any of the purposes indicated in 2 and 3? Do you favor the inclusion of *Bacillus acidophilus* preparations in New and Nonofficial Remedies?

"In answering these questions it should be borne in mind that, though products shown to be worthless are not accepted for New and Nonofficial Remedies, preparations which give promise of therapeutic usefulness are accepted; in fact, New and Nonofficial Remedies is naturally a book devoted to medicaments in the experimental stage.

"Your reply to all or any of the above questions will be appreciated."

The replies to this letter, while they have been decidedly valuable to the committee, show considerable divergence of opinion. In general it seems that the bacteriologists and scientific laboratory workers show far less enthusiasm for the claims of lactic acid bacteria to a place in practical therapy than do the clinicians. The information on many points is, however, still so vague and empirical that it is almost impossible to formulate a rational plan based on acceptable scientific evidence. In view of the enthusiasm with which the use of the products is heralded by a considerable number of clinicians, whose opinions are evidently based on empirical data, it seems advisable to the committee, pending the acquisition of further knowledge, to retain those preparations in N. N. R. for the present with a revised statement regarding their possible usefulness.

The committee's inquiries have elicited the general opinion that the Bulgarian bacilli cannot be effectively implanted in the alimentary tract by feeding cultures thereof and that it is not rational to attempt such an implantation. The overwhelming preponderance of opinion is against the usefulness of cultures of the bacilli in infected sinuses, cavities, etc.

In view of the uncertainty regarding the rôle of the *Bacillus acidophilus* the committee recommends that cultures of this bacillus be not included in N. N. R. at present.

Information from various sources indicates the importance of controlling the viability and purity of the cultures offered for sale. This the Council has done in the past and must do in the future. The committee submits a revised statement for N. N. R. 1920 with the recommendation that all descriptions of lactic acid products listed therein be made to conform therewith.

Milk soured by the accidental presence of acid-producing bacteria (buttermilk, etc.) or by the intentional addition of certain strains of bacteria with or without the association of alcohol-producing yeasts (kefir, kumyss) has been used as a food for centuries. This is due to the fact that the products were palatable to many or to a very general opinion among the laity as well as among physicians that they were advantageous for certain disorders of the gastro-intestinal tract. A great stimulus to the employment of fermented milks was given by the theories of Metchnikoff regarding intestinal putrefaction. These theories, entirely unsupported by scientific evidence, were in part that the products of intestinal putrefaction, elaborated chiefly in the large intestine, were absorbed and largely by their action on the walls of the blood vessels produced arteriosclerosis and premature senility. He also advanced the theory that the growth of the proteolytic bacteria, many of them anaerobes, which elaborated these poisons could be modified or prevented by the presence in the intestines of lactic acid-producing bacteria, especially *Bacillus bulgaricus*. No one seriously subscribes to these opinions at the present time; but, on the other hand, there is evidence that the administration of sour milk products is at times beneficial. This is particularly true in pediatrics. In this field fermented milks have found a wide application. They are used in vomiting and in acute diarrhea as well as in chronic disturbances of the gastro-intestinal tract. Under certain conditions it may be advisable to give very little fat; under others a diminution of this may not be necessary. By the use of cultures of acid-producing bacteria milk of any fat content may be fermented and the fermentation may be inhibited at any time. On what the particular value of these milks depends is not known at the present time. There can be no doubt but that a wide clinical observation gives a basis for the opinion that for certain types of gastric and intestinal disturbance fermented milk accomplishes more than sweet milk with a similar fat, sugar and protein content. Some acid-producing organisms give rise to much more uniform, smoother prod-

ucts than do others. Bacteria of the Bulgarian bacillus group, usually in association with *Streptococcus lacticus,* have been found particularly satisfactory.

There is little evidence showing that organisms of the Bulgaricus group can be implanted in the intestinal tract. They may be found in the stools so long as they are ingested in considerable numbers. As soon as the ingestion of them ceases they disappear from the stools.

There is little satisfactory proof to indicate that liquid cultures or aqueous suspensions of lactic acid-producing organisms are of value as local applications to mucous membranes or in arresting putrefaction or suppuration in wounds, abscesses and sinuses. In such conditions their use seems to be still in the experimental stage.

Sour or fermented milk may be administered in the form of buttermilk or soured skimmed milk, the lactic acid being produced by action of the paralactic acid organism *Streptococcus lacticus* which grows readily at room temperature, or in the form of sour milk produced by *Bacillus bulgaricus,* alone or in the presence of *Streptococcus lacticus.* Kefir and kumyss are produced by the action of lactic acid-producing organisms associated with an alcohol-producing yeast, which also acts on the proteins of milk and renders them somewhat more digestible.

When the ferments are administered in the attempt to cause their implantation in the intestinal tract, the Bulgarian bacillus is commonly, though without good reason, given preference, either in the form of tablets or of liquid cultures. Liquid cultures, and still more the tablets, containing the Bulgarian bacillus deteriorate with age, the deterioration being retarded by low temperatures. All lactic acid ferment preparations must be stored in an ice-chest and should be marked with an expiration date, after which they are not to be used. Bacteriologic examination of various commercial cultures and tablets has often shown them to contain few, if any, living Bulgarian organisms.

Bacillus bulgaricus belongs to a group of bacteria which has not received much scientific attention. This group is widely distributed through nature. *Bacillus bulgaricus* is a long bacillus, sometimes fairly slender and sometimes fairly thick. It has a tendency to filament formation in old cultures. It grows preferably under anaerobic conditions but grows well also under aerobic conditions. Different strains vary in this respect. Young cultures are gram-positive, but in old cultures gram-negative forms may appear. If the gram stain is applied and a red counterstain used, one filament may appear blue in some parts and red in others. Sometimes there is a tendency to granular staining if methylene blue is used. Branching is occasionally observed, the bacillus taking on the shape of the letter "Y" or "T," and thus resembling another organism of this group, *Bacillus bifidus.*

Carbohydrates are of material aid in successful cultivation of this bacillus. Broth with 2 per cent. dextrose is quite suitable for most strains, especially if calcium carbonate in the form of pieces of marble is added, so that the acid formed during growth is promptly neutralized. The medium par excellence is milk or some medium prepared from milk. Milk agar prepared by precipitating the casein and dissolving agar in the whey, is an excellent medium, especially if dextrose is added. Milk is acidified rapidly and a coagulum is formed with little separation of whey. The amount of acid formed varies with different strains, 1 to 3 per cent. or even more being attained.

Slightly different varieties of *B. bulgaricus* are used for the preparation of a milk which is usually called Bulgarian milk. In some instances the milk becomes more or less slimy; in others, the coagulum is smooth and of a creamy consistency. There should be little or no separation of whey. The delicate character and palatability of the product depends largely on the early interruption of the incubation period, and on keeping the milk at a low temperature.

The acid produced is 94 per cent. lactic acid. It has been stated that the butter fat and the casein are decomposed. If this is true the reaction is slow and the result not noticeable for several days.

The group of bacilli to which *B. bulgaricus* belongs is sometimes called "lactobacilli." They are able to multiply in the presence of a considerable amount of acid and therefore belong to the group often misnamed acidophil. They are not acidophil in the true sense of the word, but are acid-resisting. Whether we are justified in distinguishing species in this group, or only varieties, remains a subject for research. Probably the lactobacilli form a large group consisting of many varieties, as does the *B. coli* group or the group of streptococci. Research will probably show that some varieties retain their properties with tenacity, while other varieties are readily transformed. Market milk usually contains bacilli of this group. The optimum temperature for cultivation is about 45 C. Milk incubated at this temperature will, as a rule, turn very sour in the course of twenty-four to forty-eight hours and show an acidity of from 2 to 3 per cent. The lactobacilli have been considered active in the ripening of certain cheeses. They are found in the feces of man and animals. It is stated that the feces of infants can be used for the preparation of buttermilk after several transfers through milk. The Bulgarians, if they lose their "maya," which is the name of the starter for their sour milk, can replace it by using part of the stomach or intestines of a calf.

Cultures may be prepared in broth containing dextrose, or, better, in whey broth, whey agar, or in sterilized milk. Viability decreases rapidly. Frequent transfers are therefore necessary. To preserve a culture in best condition it should be transferred at least once every two days. A milk culture will contain living bacilli for many days, but their activity becomes impaired.

MERCUROCHROME—220

Preliminary Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Jan. 3, 1920, p. 31

A report on the experimental and clinical status of this new germicide for use in the genito-urinary tract by Young, White and Swartz was published in THE JOURNAL of the American Medical Association, Nov. 15, 1919. This product is prepared and marketed by Hynson, Westcott and Dunning,

Baltimore, Md., who request its acceptance for New and Nonofficial Remedies. The available evidence on Mercurochrome-220 is thus far limited to the article mentioned—obviously confirmation of the work there reported is necessary before more than a tentative acceptance can be accorded. However, Mercurochrome-220 is a definite and nonsecret compound. This, together with the evidence presented in the publication referred to, may be sufficient to warrant its use by physicians, provided, however, it is recognized that its therapeutic status is in the experimental stage. The Council has, therefore, deferred acceptance of this product for New and Nonofficial Remedies, and authorized publication of this preliminary report.

For the information of those who desire to use this compound, the following preliminary statement, based chiefly on the article by Young, White and Swartz, of its physical and chemical properties, pharmacologic actions and proposed therapeutic application is published.

W. A. PUCKNER, Secretary.

MERCUROCHROME-220.—Mercurochrome-220 is stated to be dibromo-oxymercury fluorescein.

The empirical formula is $C_{20}H_{11}O_6Br_2Hg$.

Mercurochrome-220 is described as occurring as a red powder, odorless, containing about 28 per cent. of mercury.

Mercurochrome-220 is insoluble in water, but soluble in alkalies, forming a deep cherry-red solution which fluoresces on dilution. The solution is stable in the air at ordinary temperatures, is not affected by moderate heating and does not respond to the usual tests for mercury ions. Alkaline solutions are incompatible with acids. The solution stains the skin red but the stain may be removed by rubbing first with 2 per cent. potassium permanganate solution and then with 2 per cent. oxalic solution. On ignition, Mercurochrome-220 leaves no ash.

Pharmacologic Action.—According to Young, White and Swartz, this compound is a strong and rapidly active germicide; it is active in urine, a 1:1,000 solution killing *B. coli* and *Staphylococcus aureus* in this medium in one minute. It penetrates the tissues readily. The drug is tolerated in a strength of 1 per cent. by the bladder, renal pelvis and urethra; a 2.5 per cent. solution applied to the anterior urethra caused only temporary discomfort. The toxicity, when tested by intravenous injections into rabbits, was found to be rather high, 10 Mgm. per kilo. invariably causing death within 24 hours and 5 Mgm. causing a decrease in phenolsulphonephthalein output and an albuminuria that lasted about a week. Dogs were more resistant. No systemic effects have been observed following its local application in the human.

Therapeutic Applications.—The drug has been used by Young, White and Swartz in infections of the renal pelvis, in cystitis and urethritis and in chancroidal ulcerations. In the treatment of infections of the kidney pelvis, the ureters were catheterized and the pelvis gently filled with a 1 per cent. solution of the drug; the catheter was plugged and the solution retained in the pelvis for five minutes. In the treatment of bladder conditions, one ounce of the 1 per cent. solution was introduced into the bladder and retained for one hour or longer, the treatment being given daily or on alternate days or at longer intervals according to circumstances. In anterior gonococcus urethritis, the anterior urethra was filled with a 1 per cent. solution and retained for five minutes; if the posterior urethra was involved, the solution was gently forced into the posterior urethra and bladder and retained for an hour or more.

Later, in the treatment of acute anterior gonorrhea, 2.5 per cent. solution[1] was used every three hours. In the case of chancroidal ulcerations, the drug was applied as a moist dressing (1 per cent.) or as a starch paste (5 per cent.) or as an ointment (5 per cent.).

The results have been satisfactory and no untoward effects observed. Cases of long-standing, purulent cystitis have cleared up in a few days; in the case of gonorrhea, the discharge became free of the organisms in from three to seventeen days, the average being ten. The chancroidal ulcerations cleared off in from one to four days.

"ANTI-PNEUMOCOCCIC OIL" AND THE USE OF CAMPHOR IN PNEUMONIA

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Jan. 3, 1920, p. 46

The Council has adopted and authorized publication of the report which appears below. This report declares "Anti-Pneumococcic Oil" (a solution of camphor in oil sold by Eimer and Amend, New York) ineligible for New and Nonofficial Remedies because (1) the recommendations for its use in pneumonia are not warranted by the evidence, (2) the name is not descriptive of its composition but is therapeutically suggestive, and (3) the sale of a solution of camphor in oil under a name nondescriptive of its composition is unscientific and a hindrance to therapeutic progress.

W. A. Puckner, Secretary.

The Council having decided to consider Anti-Pneumococcic Oil (Eimer and Amend, New York), the preparation was assigned to the Committee on Therapeutics for report. The report that follows was made by a member of this committee:

According to the advertising, Anti-Pneumococcic Oil is a "twenty-five per cent. solution of camphor in a thin oil" which was "originated" by August Seibert, M. D. The following directions are given for its use:

"10 c.c. (150 minims) to every 100 pounds of body weight, to be injected hypodermically every eight to twelve hours in pneumococcic pneumonia, as soon after the initial chill as possible."

It is claimed that the prescribed dose one hour before general anesthesia begins, "safeguards against postoperative pneumonia," and, that "animals can so be immunized against later and otherwise fatal intravenous pneumococcic infection (Boehnke, Institute for Experimental Therapy, Frankfort)." The advice is given:

"In pneumococcic meningitis, endocarditis and pleuritis, 3% of salicylic acid should be added to this oil."

In an article by Seibert, "Camphor and Pneumococci" (*Medical Record,* April 20, 1912), a reprint of which is used to advertise Anti-Pneumococcic Oil, previous work (*München. med. Wchnschr.,* No 36, 1909) is mentioned as the starting point for the use of camphor in pneumonia. In this article, the author reports his first case, that of a young woman who entered St. Francis' Hospital on the third day after the initial chill "with the symptoms of severe toxemia (unconscious, temperature 105.5 F., pulse 130, and respiration 40) and involvement of both lower lobes." "Large doses of camphor," 12 c.c. of a 20 per cent. solution, were injected hypodermically "every twelve hours, resulting in *gradual* improvement and recovery by the fourth day, without a crisis." Seibert reports success in its use in twenty-one cases, but gives no case histories or protocols. He admits, however, that in four out of sixteen cases, following the first twenty-one so reported certain "limitations of this treatment were observed," and a "sudden rise of temperature in two patients on the second and third days of treatment, respectively, proved to be due to pneumococcic nephritis, promptly subdued by appropriate doses of urotropin, while the camphor injections were continued and resulting in speedy recovery." He further admits that empyema occurs, and states: "This proves that the camphor brought into the blood cannot prevent the as yet living organisms, constantly entering the blood current from the affected alveoli, from colonizing in the renal and pleural tissue."

He reports, among thirty-seven patients treated in this manner, one death, that of a man 68 years old, weighing 200 pounds, with a fatty heart. Heart failure was the real cause of death. Seibert also reports some very incomplete

experimental work; Dr. Hensel, assistant and pathologist of the German Hospital, found that "1/10,000 part of camphor added to the usual culture media inhibited the growth of pneumococci, while the controls all thrived"; Dr. J. C. Welch, pathologist of the Lying-In Hospital, found that rabbits infected with lethal doses of pneumococcus cultures intravenously were saved by large doses of camphorated oil; fragmentary protocols are given. The assistant pathologist of St. Francis' Hospital carried on the experimental work, adding salicylic acid to the camphor. No blood cultures are reported. The conclusion reached by Dr. Seibert is that salicylic acid up to 3 per cent., added to the camphorated oil, is effective in preventing pleural infection. In the article by Dr. Seibert, there appear most sketchy reports of cases, recovery being reported without crisis in from three to nine days.

The referee has made a careful search of the literature, with the following results: Boehnke (*Berl. klin. Wchnschr.* **50**:818, 1913), using white mice, failed to confirm the experiments reported in Seibert's paper, unless camphorated oil were given before the pneumococci, and even then, he felt that the results were too irregular to be of great significance. When given with anti-pneumococcic serum, however, he felt that there was some benefit to be seen by the administration of camphor; his protocols, however, are not detailed. There is no report of blood cultures, etc.

Another worker, H. Leo (*Deutsch. med. Wchnschr.* **39**:690, 1913), reported that camphor water given intravenously prolonged the lives of thirty-eight rabbits inoculated with pneumococci. Here again there were no adequate protocols and very little evidence of careful experimental work appears.

In the literature of the past ten years, there appear sketchy clinical articles on the value of huge doses of camphor in pneumonia. Markevitch (*Russk. Vrach,* June 27, 1914; abstr., THE JOURNAL, Dec. 5, 1914, p. 2081) treated 226 cases of pneumonia with 5 c.c. of camphorated oil hypodermically four times daily, at the same time giving digitalis (amount not stated), with a mortality of 6.6 per cent., whereas, in 322 cases untreated, there was a mortality of 13.3 per cent. He reports 133 grave cases; sixty-six received no camphor; 48 per cent. died. Of sixty-seven treated with camphor, only 22 per cent. died. He reports temperature falling by lysis when camphor is used, and comments on the symptomatic improvement following its use. With the great variation in the clinical course of pneumonia, the above figures, though suggestive, certainly need further support before

the routine use of camphor as recommended by Seibert can be sanctioned.

Later articles found on the subject refer to it in a very cursory way, giving no protocols and no cases, and giving the referee the feeling that the conclusions were very impressionistic.

RÉSUMÉ

After careful search of the literature, the referee concludes that: Huge doses of camphor, to 250 grains in twenty-four hours, may be given to man without serious results. No satisfactory evidence, however, appears that camphor has a specific germicidal action on pneumococci (similar to that of ethylhydrocuprein). The clinical evidence, as found in the literature, is certainly of very little value. It appears that the sale of a simple solution of camphor in oil under the guise of "Anti-Pneumococcic Oil" is to be deplored (a 20 per cent. solution of camphor in cottonseed oil is official in the U. S. Pharmacopeia as camphor liniment). It is recommended that the preparation be held inadmissible to New and Nonofficial Remedies because exaggerated therapeutic claims are advanced for it, and because the name is not descriptive of the composition, but is, instead, therapeutically suggestive.

DIAL "CIBA"

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Jan. 24, 1920, p. 265

Dial "Ciba" has not been accepted for "New and Nonofficial Remedies" because, as the report which follows shows, unwarranted claims are made for the product. It is a definite new chemical compound which might be made eligible for N. N. R. if misleading therapeutic claims were eliminated. The Council directed that Dial "Ciba" be included with Articles Described but Not Accepted, so that physicians might be informed with regard to its character and properties.

W. A. Puckner, Secretary.

Dial "Ciba" is a hypnotic manufactured by the Society of Chemical Industry of Basle, Switzerland, and is sold in the United States by A. Klipstein and Company, Inc., New York. Chemically, Dial "Ciba" is diallylbarbituric acid and is, therefore, closely related to diethylbarbituric acid or barbital ("veronal").

The claims made for Dial "Ciba" are (1), that the "allyl" group in its molecule makes it more readily decomposed by oxidizing agents than barbital, which contains the "ethyl"

group; (2) that because of this ease of oxidation, it is more readily decomposed in the body and more rapidly and completely eliminated, and (3) that because of its alleged rapid elimination, it is devoid of the after effects of barbital and other hypnotics.

The Council took up the substance in February, 1918, and referred the matter to the referee in charge of barbital preparations. The referee considered unwarranted the claim that Dial "Ciba" did not have the after-effects of other hypnotics due to its alleged total decomposition in the body. The American agents, A. Klipstein and Company, were informed of the referee's objections. Their attention was also called to the fact that, nothwithstanding the claimed absence of after-effects in one part of the advertising, other parts of the same advertising admitted certain post-hypnotic effects of the product. It was pointed out also that while it was claimed in one of the advertising circulars that lowering of the blood pressure is never observed after administration of Dial "Ciba," yet two of the authors quoted in the same circular definitely stated that a lowering of the blood pressure followed even small doses of the drug and these authors warn against this very danger in certain conditions.

A year later, a circular letter sent out by A. Klipstein and Company reiterated the claim that the asserted decomposition of Dial "Ciba" in the body prevents after-effects, the drug being still contrasted with barbital ("veronal"). In view of the reiteration of this highly improbable claim, the referee undertook to study the comparative action of Dial "Ciba" as compared with other hypnotics. It was found that the actions of Dial "Ciba" are not distinguishable, qualitatively, from those of barbital, there being no perceptible difference in the after-effects or in the nature of the side actions. In toxic doses, both caused profound depression with the temperature falling to that of the room (or about one degree above), the respiration being extraordinarily slow and shallow as one would expect with lowering of the temperature. There were also the same evidences of nausea that are so frequently seen after toxic doses of the various hypnotics of this group. In view of these results, the Council declared that it is unwarranted to claim freedom from after-effects for Dial "Ciba."

The Council held that the following statement is unwarranted:

"The therapeutic field for Dial 'Ciba,' as shown by tests on rabbits, is just as broad as the field for Diethylbarbituric Acid."

Tests on rabbits do not and cannot show the breadth of the therapeutic field for a hypnotic. The Council also declared

the following statement improbable, and contrary to the evidence obtained by the referee:

"In dogs, the increase of dosage beyond the therapeutic dose to the point of death is decidedly in favor of Dial 'Ciba,' which required a larger dose [than diethylbarbituric acid] to produce death."

The referee's experiments on cats show that Dial "Ciba" is several times as toxic as hydrated chloral, and more than twice as toxic as diethylbarbituric acid (barbital).

Since the circular to which objection was made in 1918 was still being sent out in December, 1919, the Council held Dial "Ciba" inadmissible to N. N. R. and voted that report of its action in the matter be authorized for publication. The Council further directed that Dial "Ciba" be included with Articles Described but Not Accepted.

APOTHESINE

Report of the Council on Pharmacy and Chemistry

From The Journal A. M. A., Jan. 24, 1920, p. 266

Apothesine is a synthetic drug for producing local anesthesia, made by Parke, Davis & Company. In the fall of 1917 the Council wrote to Parke, Davis & Company offering its aid in establishing the identity, purity, and therapeutic efficiency of this synthetic local anesthetic with the ultimate object of accepting the product for inclusion in New and Nonofficial Remedies should the facts warrant such acceptance. The Council's letter was never acknowledged. After Apothesine was put on the market the Council desired to accept it for inclusion in New and Nonofficial Remedies but, unfortunately, was unable to do so because some of the claims made for the product were not justified by acceptable evidence. The manufacturers were notified of the Council's desire to admit this product to N. N. R. and the wish was expressed that the company would either so modify its claims as to make the product acceptable under the Council's rules or else would submit evidence to the Council in proof of the claims made and thus permit the Council to revise its conclusions. Parke, Davis & Company were, apparently, either unwilling or unable to submit evidence that would sustain their claims; neither did they offer to modify the claims themselves. The product, therefore, is ineligible to inclusion in New and Nonofficial Remedies; it will, however, be listed in the "Described But Not Accepted" department of New and Nonofficial Remedies. The report on Apothesine that follows has been authorized for publication.

W. A. Puckner, Secretary.

Apothesine, "the hydrochlorid of diethyl-amino-propyl-cinnamate," is an efficient local anesthetic. It belongs to the procain rather than to the cocain type, that is, it belongs to that type which, while effective for injection anesthesia (especially when combined with epinephrin) is relatively inefficient when applied to mucous membranes. Apothesine may also be used for spinal anesthesia. Its absolute toxicity is less than that of cocain (as 20 is to 15, see table below) but about twice that of procain (as 20 is to 40, see table below). It is non-irritant, is easily soluble and makes a stable solution so that it may readily be sterilized.

The Council took exception to certain claims made by Parke, Davis & Company for their product on the ground that these claims were not supported by acceptable scientific evidence. One of the claims was that Apothesine is applicable in any case in which any other local anesthetic is used. This statement, made in many advertisements, is distinctly misleading as used. When applied to mucous membranes Apothesine is far inferior to cocain and to some other local anesthetics, yet the claim obviously suggests that Apothesine is an efficient substitute for any local anesthetic.

The manufacturers claimed, too, that Apothesine is as potent as cocain. The claim would lead the physician to think that Apothesine had the same anesthetic potency as cocain in solution of equal strength. This statement, so far as it refers to the drug when applied to mucous membranes, is not in accord with the facts and is true for injection anesthesia only when stronger solutions are used. The only support for the claim of equal efficiency appears to be the experiments with intracutaneous injections made by H. C. Hamilton[1] in Parke, Davis & Company's laboratory. These differed considerably from the results of Sollmann.[2] A further series of experiments were made by Sollmann to compare still further the diverse results previously reported by him and Hamilton. The latest series, while showing considerable variations in the susceptibility of different skin areas, especially toward Apothesine, demonstrated in every case that the efficiency of Apothesine is unmistakably lower than that of cocain, being at best one half. The series also showed that the potency of Apothesine was never greater than procain and averaged considerably below it.

1. The Comparative Values of Some Local Anesthetics by H. C. Hamilton, Detroit, Mich., from the Research Laboratory of Parke, Davis & Co., J. Lab. & Clin. M. **4**: 60 (Nov.) 1918.

2. Comparative Efficiency of Local Anesthetics, V, by T. Sollmann, from the Pharmacological Laboratory of the School of Medicine, Western Reserve University, J. Pharmacol. & Exper. Therap. **11**: 69 (Feb.) 1918.

Another claim made for Apothesine which the Council holds is not supported by evidence is that of superior safety. This claim is made on the basis of hypodermic injections in guinea-pigs carried out in the laboratory of Parke, Davis & Company. Such experiments prove little because of the fact—well known to laboratory workers—that the use of rodents in toxicity tests made by injecting a drug into the subcutaneous tissues does not give a reliable index of the relative toxicity of such a drug for man. This is due partly to the peculiar resistance of rodents to poisons and partly to the great importance of the rate of absorption. The organism destroys most local anesthetics so rapidly that the rate of absorption is more important than the absolute dose. The absorption from hypodermic injections into guinea-pigs differs, of course, from that in clinical accidents, especially where the drug has been applied to mucous membranes. One cannot, therefore, reliably estimate the degree of clinical danger on animals.

It has been shown that when toxicity tests of local anesthetics are made on cats these animals seem to respond to the drugs in a manner more closely approximating humans and it is a suggestive fact that the more toxic of local anesthetics, as shown by tests on cats, have been found the most dangerous in clinical use. The *absolute* toxicity of Apothesine has been measured by Eggleston and Hatcher[3] by the intravenous injection in cats. The fatal doses, in terms of milligrams per kilogram ranged as follows:

Alypin, Holocain	10
Beta Eucain	12.5
Cocain	15
Apothesine	20
Tropacocain	20—25
Stovain	25—30
Nirvanin	30—35
Procain	40—45

The *absolute* toxicity of Apothesine is, therefore, only a little lower than that of cocain, and is twice as great as that of procain. The *clinical* dangers cannot be predicted by either method, since clinical accidents depend, in most instances, on idiosyncrasies, or the technic of application.

3. A Further Contribution to the Pharmacology of the Local Anesthetics by Eggleston and Hatcher, from the Department of Pharmacology, Cornell University Medical College, New York City, J. Pharmacol. & Exper. Therap. **13**: 433 (Aug.) 1919.

ALKALITHIA

Report of the Council on Pharmacy and Chemistry

Alkalithia was introduced at a time when it was believed that the administration of lithium salts served to remove uric acid from the system. The product was considered by the Council in 1906, and found ineligible for New and Nonofficial Remedies. No report, however, was published at that time.

Because of inquiries received, the Council examined the current claims for Alkalithia, and authorized publication of the report which appears below.

W. A. PUCKNER, Secretary.

Keasbey and Mattison Company's Effervescent Alkalithia is sold with the following statement of composition:

"Each dose or heaping teaspoonful contains 1 grain of Caffeine, 10 grains each of Bi-carbonates of soda and potash, and 5 grains of Carbonate of Lithia."

The A. M. A. Chemical Laboratory reports that Alkalithia is an effervescent mixture which contains alkaline carbonates and bicarbonates together with caffein, free tartaric acid and free citric acid. The major portion of the alkali carbonates and bicarbonates is converted into citrates and tartrates when the preparation is dissolved in water—as is done before it is taken. An excess of alkali is present, however, as the solution has an alkaline reaction. Each "heaping teaspoonful" (which was found to be about 4.85 Gm.) contains about 0.044 Gm. of caffein (the manufacturers claim 0.0648 Gm. per heaping teaspoonful). As taken, Alkalithia, therefore, represents caffein in a solution of alkali tartrate, citrate and bicarbonate containing free carbonic acid. If it is assumed that all of the tartrate and citrate in Alkalithia is converted into carbonate in the organism, a "heaping teaspoonful" of Alkalithia would represent about 2.9 Gm. of sodium bicarbonate. This assumption is, however, not correct, for it is known that tartrates are not completely converted into carbonates in the organism.

According to the label on the bottle, this mixture of caffein and alkali salts is "a common sense remedy for the relief and treatment of conditions dependent upon perverted metabolism as manifested by neuralgic, rheumatic, cardiac and renal symptoms." Wrapped with a trade package is a circular in which is discussed the "uric acid diathesis" as "a cause of Rheumatism in its various forms, Calculus, Gravel and Inflammation of the Bladder and Kidneys, Asthma, Hay

Fever, Catarrh, Quinsy and Bronchitis, Eczema, Hives, Itching and Burning of the Skin, Palpitation of the Heart and Cold Hands and Feet, Dizziness, Mental Depression, Melancholia, Neuralgia, Chorea, Hysteria, Numbness and a great variety of purely nervous symtoms." The arguments for the use of Alkalithia as "a safe and scientific treatment for the uric acid diathesis" found in the circular constitute an indirect appeal to the laity (conflict with Rule 4).

In the circular matter sent direct to the physicians, Keasbey and Mattison claim that in rheumatism, Alkalithia is prescribed by the medical profession more often than any other remedy. The claim is made that, "In five minutes the urine will be discolorized and analysis will show it to be loaded with urates." The manufacturers further assert:

> "You can change the character of the urinary secretion in a few minutes completely" by Alkalithia, and "In nine cases out of ten, when the doctor prescribes 'Alkalithia' his patient greatly improves, or gets well."

The firm advises that "Renal Insufficiency" be determined by the old method of multiplying the ounces of urine in twenty-four hours by the last two numbers of the specific gravity, adding 10, which gives the number of grains of solids excreted in the twenty-four hours. If this is low, no matter what the cause, they advise Alkalithia, "that ideal eliminant."

The Council declared Alkalithia inadmissible to New and Nonofficial Remedies because the claims made on the label and the circular accompanying the trade package lead the public to its detriment to depend on this preparation (Rule 4); and because the therapeutic claims are unwarranted (Rule 6).

ARHOVIN OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

Arhovin is a solution of dephenylamine, thymol benzoate and ethyl benzoate, marketed by Schering and Glatz, Inc. It was omitted from New and Nonofficial Remedies because the therapeutic claims made for the preparation were unwarranted and because the firm had refused to discontinue the distribution of the advertising which contained the objectionable claims prior to Jan. 1, 1919. When the report which appears below explaining the dismissal was submitted to Schering and Glatz, Inc., the firm again promised a revision

of its advertising, but refused discontinuance of the objectionable circular before Jan. 1, 1920. Since Arhovin is still marketed with unwarranted therapeutic claims, the Council has authorized publication of this report.

W. A. PUCKNER, Secretary.

The attention of the firm Schering and Glatz, Inc., was called to misleading statements in its booklet for Arhovin in 1915, and in 1918 the firm was informed that unless the misleading statements were withdrawn before Jan. 1, 1919, Arhovin would be omitted from New and Nonofficial Remedies.

The following quotations are taken from the circular in question, and illustrate the character of the claims to which objection was made:

"Striking also is the antiphlogistic and anesthetic effect of Arhovin on the inflamed mucosae, an effect which, as all authorities agree, is far greater than that of all other internal antigonorrheaics."

"Under its influence vesical and prostatic complications, gonorrheal arthritis, endocarditis, etc., are rarely incurred."

References to the indexes of leading textbooks, including those of Meyer and Gottlieb, Cushny, Sollmann and Bastedo, fails to show that Arhovin is so much as mentioned by those authors; hence, it is obviously false to state, as is done in the first of the quotations above, that all authors agree concerning the striking effects of Arhovin.

Many of the statements are objectionable by reason of the actions implied, rather than stated directly. The following are examples:

"Arhovin in Gonorrheal Infections of the Male Genito-Urinary Organs. Anterior Urethritis. This is the class of cases in which the most favorable results from Arhovin have been reported."

"Posterior Urethritis.

"Here also the striking effects from Arhovin medication, both in acute and chronic cases, are rapid decrease of discharge, disappearance of gonococci from the secretion, and cessation of subjective difficulties, such as strangury."

While the firm did not agree to withdraw the objectionable advertising before Jan. 1, 1919, which made necessary the omission of Arhovin from New and Nonofficial Remedies, 1919, it did submit a proposed folder in which the most objectionable of the claims are still made.

The following statement, which was in the proposed "folder" and is included in an advertising pamphlet sent out during 1919, serves to illustrate those points:

"Its action is three-fold:

"Strong antiseptic and bactericidal effect upon the urethral and vesical mucosae, highly conducive to shortening and palliation of the acute disease course."

No evidence has been presented that Arhovin is capable of destroying the gonococcus in the urethra, and consequently, the Council declared the recommendation for the use of Arhovin in the treatment of gonorrhea, by means of claims such as those just cited, is both misleading and dangerous.

BENZIDINE BRANDS AND DOSAGE FORMS AND FERMENTDIAGNOSTICUM NOT DESCRIBED IN NEW AND NONOFFICIAL REMEDIES

Report of the Council on Pharmacy and Chemistry

The Council has decided that those reagents used outside the body which are now in New and Nonofficial Remedies be omitted when their period of acceptance expires.

The three-year term of acceptance having expired for the brands and preparation of benzidine and for fermentdiagnosticum, the Council directed that they be omitted from future editions of New and Nonofficial Remedies. As a matter of record, the descriptions have been referred to the Council reports and appear below.

W. A. PUCKNER, Secretary.

BENZIDINE. — Para-diamino-diphenyl. — For description see the U. S. Pharmacopeia under Reagents and Test Solutions.

Benzindine-Merck (For Blood Test). — A nonproprietary brand complying with the standards for benzidine.

Merck & Co., New York, distributors.

Occult Blood Test (Dudley Roberts).—This consists of tablets each containing 5 grains of a trituration of benzidine, 1 part, and sodium perborate, 20 parts, and glacial acetic acid (supplied in boxes containing 100 tablets in vials, and a bottle of glacial acetic acid).

Actions, Uses and Dosage.—A tablet is placed in a small saucer or other suitable container; to it is added a quantity of the material to be tested (a weak solution of the stool

or stomach contents, or urine), sufficient to wet thoroughly, but not to cover the tablet entirely, and then a drop or two of the acetic acid is allowed to fall on the tablet; if blood is present the tablet will turn greenish blue, the extent of the coloration and the time of its development depending on the amount of blood present. (To avoid contamination of the glacial acetic acid remaining in the bottle, care should be taken not to touch the tablet or specimen with the rod which is used to transfer the acetic acid for the test.)

Prepared by E. R. Squibb & Sons, New York. No U. S. patent or trademark.

FERMENTDIAGNOSTICUM — Solution of Glycyltryptophan-Kalle.—A specially prepared solution of glycyltryptophan for use in determining the presence of a peptolytic ferment.

Actions and Uses.—Glycyltryptophan is decomposed in the presence of certain ferments into tryptophan and glycin (amino-acetic acid). The presence of tryptophan is determined by the characteristic test for that substance. If tryptophan is found in the solution after incubation with a suspected solution (stomach contents) it is concluded that a peptolytic ferment was present in the substance tested.

As peptolytic ferments are not present in stomach contents except after regurgitation from the intestine or in the presence of cancer, it is claimed that fermentdiagnosticum may be applied as a test for the diagnosis of cancer in the stomach. Since, however, it appears that the saliva of some individuals contains a ferment capable of splitting glycyltryptophan and since, according to some, the ferments of a gastric carcinoma are not found in the gastric contents unless the tumor is undergoing ulceration, the test has a number of limitations which diminish its value.

Dosage.—Each bottle contains a quantity sufficient for one reaction, the solution being covered with toluene for preservation. The material to be tested should be examined for bile and blood and tested with bromine water or bromine fumes for the presence of tryptophan. If these tests give negative results the stomach fluid is suitable for the application of the fermentdiagnosticum.

The bottle is filled to the mark with filtered stomach contents and placed in the incubator for twenty-four hours. It is then taken out and from 2 to 3 Cc. of the solution underneath the toluene layer are removed and tested for the presence of tryptophan.

Manufactured by Kalle & Co., Biebrich a/Rh., Germany (Kalle Color & Chemical Co., Inc., New York). German trademark. No U. S. patent or trademark.

CHLORON, CHLORAX AND NUMBER "3"

The report which appears below was sent to the Chlorine Products Company, Inc., May 14, 1919. In reply to an inquiry sent the Chlorine Products Company, July 8, the company wrote that it could send no reply because the medical director was still in France. However, Chloron and Chlorax are being advertised in medical journals; also essentially the same advertising as that discussed in the report was recently received by a physician from the Chlorine Products Company.

The preceding facts having been reported to the Council, publication of the report was authorized.

W. A. PUCKNER, Secretary.

Chloron, Chlorax and Number "3" are preparations of essentially similar composition put out by the Chlorine Products Company, Inc., New York.

Chloron

Chloron, according to the label, is "A stable CHLORINE remedy for the reduction of inflammation, relief of pain and for all wounds, burns, scalds and every description of sores except cancer and lupus." Its composition is given as:

"Free chlorine, 0.200 per cent.; Calcium chloride, 0.190 per cent.; mercurous chloride, 0.030 per cent.; lithium chloride, 0.035 per cent.; calcium hydrate, 0.010 per cent.; water to 100 parts."

The Council asked the manufacturers for further information in regard to the composition or preparation of Chloron and received this reply:

"Chlorine gas is prepared in the usual way and purified and passed into water until a saturated solution is made.

"Water to the extent of three times the volume of the chlorine solution is used to dissolve the necessary amount of calcium chloride, and the two solutions are mixed.

"The necessary amounts of Lithium and Mercurous Chloride are then intimately mixed and made into solution. This solution is then added to the above and the whole is agitated for some minutes."

A specimen of Chloron was examined in the A. M. A. Chemical laboratory and the chemists reported:

Qualitatively the presence of the following constituents was confirmed: calcium, mercury, lithium, chlorid, free chlorin. The solution was alkaline. Of course, the declaration that Chloron contains mercurous chlorid (calomel) is obviously incorrect, as mercurous chlorid cannot exist in a solution containing active (free) chlorin, but is oxidized to mercuric chlorid (corrosive sublimate). As the solution was alkaline in reaction, it seemed unlikely that all the active chlorin was present in the free state, as declared on the label.

Quantitative determination of free chlorin and of total active ("available") chlorin gave: free chlorin, 0.036 gm. per hundred c.c.; total "available" chlorin, 0.330 gm. per hundred c.c., or 165 per cent. of the claimed amount.

A comparison of the information sent to the Council with the analytic findings leads to the conclusion that Chloron is not of reliable composition.

As evidence of the therapeutic value of Chloron, the following "case reports" were submitted:

"In a case of second degree burn involving the most of one leg from the middle of the calf down, CHLORON was the only dressing used. The burn was a bad one and the patient in a rundown anaemic condition, at no time was there any appearance of pus, the surface looked clean and bright and the healing was accomplished with practically no scar whatever. The burn was kept wet with the solution by hourly applications day and night. The skin which has grown on the wound is clear, healthy and firm.

In another case of Varicose veins of long standing, the result was surprising. The patient told of two years vibrating from Hospital to Hospital and getting no real relief. Each leg had large open running sores, the only dressing used was wet compresses of this solution. The pus disappeared at once, the wound began to cicatrise from the edges and in two weeks the man was discharged from the hospital practically cured."

"CHLORON was recently tried at the —— and —— Hospital on cases presenting ulcers and other sores which did not readily yield to other methods, with good results, in fact were of an indolent type. In these cases CHLORON proved very valuable."

"I have used CHLORON on a series of cases (surgical) presenting pus foci and I have found the application very beneficial and healing, the pus early disappearing. In cases of Osteomyelitis, Suppurating Arthritis, Cellulitis and Chronic Ulcers, CHLORON is particularly valuable, its good effects quickly observed and the time of restoration to health shortened."

In the first case report, there is no evidence that Chloron is more efficient in the treatment of burns than any other commonly used procedure might have been. In the case of the varicose ulcers, while there was some apparent benefit from Chloron, no credit is given to rest and the general treatment which is known to be important in the treatment of such conditions. The evidence in the other case reports is quite inconclusive. Consideration of the "case reports" leads to the conclusion that clinical evidence for the value of Chloron is lacking.

Attention should be called to the fact that the amount of active chlorin, claimed to be present in Chloron as well as the amount found by the association laboratory, is less than that considered effective by Dakin, Dunham and others; seemingly in preparing Chloron no attention has been paid to the degree of alkalinity, yet the importance of this factor is now generally recognized.

Chloron fails to comply with the requirements for surgical solution of chlorinated soda (N. N. R., 1919, p. 133), yet the manufacturers make free use of the text of Dakin and Dunham's Handbook of Antiseptics in their advertising pamphlet. Thus:

From the Chloron pamphlet:

"This ideal antiseptic effects complete sterilization within its sphere of action without causing any damage to the cells or tissues. An important method of judging the injurious action of antiseptics is to investigate their effects on the leucocytes. From experiments *in vitro* by Parry Morgan and *in vivo* by Col. C. J. Bond with the strength of antiseuptics commonly used in surgery, it has been found that Chlorine antiseptics and mercury salts have little effect on phagocytosis in comparison with other germicides.

The activity of the leucocytes from wounds which have recently been treated with CHLORON may be demonstrated experimentally."

"In addition to its antiseptic action CHLORON is a strong oxidizing agent and deodorant and possesses to a marked degree the property of decomposing toxins. In this connection it is interesting and pertinent to note that Dean, by the regulated action of hypochlorous acid, has prepared a nontoxic dysentery vaccine and it is now a common observation that the free use of CHLORON may reduce the constitutional symptoms arising from septic processes and that they reappear on discontinuing the antiseptic treatment."

Dakin and Dunham Handbook of Antiseptics:

"The ideal surgical antiseptic should effect complete sterilization within its sphere of action without causing any damage to animal cells. At the moment such a substance does not appear likely to be found, but on the other hand it is surprising to see how little damage may be done to animal tissues by some active antiseptics. An important method of judging of the injurious action of antiseptics is to investigate the condition of the leucocytes in wounds recently treated with the substance under consideration. In general it appears from experiments *in vitro* that, with the strength of antiseptics commonly used in surgery, mercury salts and hypochlorites have relatively little effect on phagocytosis as compared with phenol (Parry Morgan). It is a regular phenomenon to observe activity of the leucocytes obtained from wounds which have been recently treated with hypochlorites.

Ingenious methods for determining the influence *in vivo* of antiseptics on the activities of leucocytes have been worked out by Col. C. J. Bond."

"In addition to their disinfecting action, the Chlorine antiseptics are strong oxidizing agents and deodorants and moreover possess in high degree the property of decomposing toxins. By the regulated action of hypochlorous acid, Dean has prepared a nontoxic dysentery vaccine and it is a common observation that the free use of hypochlorites may reduce the constitutional symptoms arising from septic processes and that they reappear on discontinuing the antiseptic treatment."

Chlorax

Chlorax is said to be "A stable CHLORINE solution for internal use," in "Kidney Conditions," "Diabetes," "Acute Infections," "Blood Dicrasias," "Lithemias and Rheumatism," and

"Nervous Conditions." It is claimed to have the same composition as that of Chloron with the addition of 0.016 per cent of tincture of opium.

The A. M. A. Chemical Laboratory reported that the free chlorin in Chlorax was 0.01 gm. per hundred c.c. and the total amount of active ("available") chlorin was 0.25 gm. per hundred c.c., or 125 per cent. of the amount claimed. The laboratory notes that though the chlorin content of Chloron and Chlorax is claimed to be the same, that of Chlorax actually is less. This is not surprising when the presence in Chlorax of reducing substances such as alcohol is borne in mind. The laboratory concludes that Chlorax is not of reliable composition.

The following is typical of the "case reports" submitted to show the value of Chlorax:

"In January last I used Chlorax on a case of Diabetes Mellitus and with excellent results.

"The patient had been suffering for about nine years and when first brought to my care Toxemia had set in, he was drowsy, irritable and unable to leave the house. I prescribed Chlorax in teaspoonful doses four times a day and am pleased to say that in one week he showed marked improvement. Soon after he was able to leave the house and attend to his business and after two months treatment resumed a normal diet and habits apparently without injurious effects.

"I believe that in this case Chlorax undoubtedly prolonged life."

No mention is made of the dietary or other measures used. The wide variation in diabetes and its response to proper diet is so well known that the noncommittal statement concerning the beneficial effects of Chlorax amounts to no evidence at all in favor of the preparation.

The other "case reports" furnished by the Chlorine Products Company, Inc., which concern the treatment of gastric ulcers, acute alcoholic gastritis, tonsillitis, etc., are equally unconvincing. In fact, no satisfactory evidence for the clinical value of Chlorax has been presented.

The following from the advertising for Chlorax is unwarranted and absurd:

"Mercurous chloride (calomel) is perhaps the most widely used internal antiseuptic and alterative and has established itself in the therapy of constipation, cholera, dysentery, cardiac dropsy, pleurisy, malignant fever, malaria, syphilis, worms, infectious diseases, gout and rheumatism; lithium chloride is particularly efficacous in acute and chronic parenchymatous nephritis and in various lithemic conditions; while Opium has no rival as an anodyne and can be used to stabilize and conserve the alkaline reserve of the body against the acidosing influence of infections."

Further, on page 14 we find:

"In chills and fever, malaria and other blood dicrasias, CLORAX is indicated as an internal antiseptic and it exerts a beneficial effect on the course of these diseases."

The claims made for Chlorax are exaggerated and misleading.

Number "3"

According to the label, Number "3" is "A STABLE CHLORINE remedy for the purification of the blood," with the composition:

"Free Chlorine, 0.35 per cent.; Calcium Chloride, 0.30 per cent.; Mercurous Chloride, 0.03 per cent.; Lithium Chloride, 0.04 per cent.; Calcium Hydrate, 0.01 per cent.; Opium, 0.02 per cent.; Ethyl Alcohol, 0.10 per cent.; water to 100 parts."

It will be noticed that the composition claimed for Number "3" is essentially similar to that claimed for Chloron. It differs from Chloron in that the amounts of some of the constituents are somewhat greater, and in that, like Chlorax, it contains some tincture of opium.

The A. M. A. Chemical Laboratory reports that the free chlorin in a specimen of Number "3" was 0.024 gm. in 100 c.c. and the total active ("available") chlorin 0.173 gm. per hundred c.c., or about 50 per cent. of the claimed amount. The examination indicates that Number "3" is of unreliable composition. The Chlorine Products Company, Inc., submitted no clinical evidence for Number "3" to which it refers as "our Syphilis remedy." It stated that two physicians had used the preparation "with good results," and admitted that "the company requires further evidence before pushing it."

The Council declared "Chloron," "Chlorax" and "Number '3'" in conflict with the rules governing admission to New and Nonofficial Remedies. All are of unreliable composition (conflict with Rule 1). The therapeutic claims made for the preparations are not substantiated by acceptable evidence and are unwarranted and misleading. Chloron is inferior as an antiseptic to the well-known surgical solution of chlorinated soda on account of its low chlorin content and uncontrolled reaction. There is no warrant for the claim that Chlorax is useful in the treatment of "Kidney Conditions," "Diabetes," "Acute Infections," "Blood Dicrasias," "Lithemias and Rheumatism," and "Nervous Conditions," nor is there warrant for the claim that "Number '3'" is a remedy for the purification of the blood or a "Syphilis remedy" (conflict with Rule 6).

The names of these pharmaceutical mixtures are not descriptive of their composition (conflict with Rule 8).

All three preparations are irrational. No evidence has been furnished that the lithium salt is of value in the mixtures. It is not rational to combine an active chlorin preparation

and a mercury salt in one mixture, nor is there evidence that the addition of opium to the preparations proposed for internal use is of value or rational. Experimentation with Number "3" as a "Syphilis remedy" is to be severely condemned in that those on whom it is used will in the meantime be deprived of efficient medication (conflict with Rule 10).

ELARSON OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report announcing the omission of Elarson from New and Nonofficial Remedies.

W. A. Puckner, Secretary.

Elarson, now sold by the Winthrop Chemical Company, Inc., was formerly sold in the United States by the Bayer Co., Inc. It was admitted to New and Nonofficial Remedies in 1914.

The circular issued by the Winthrop Chemical Co. contains several statements markedly at variance with the results of an investigation made, at the request of Fischer, by Joachimoglu (*Arch. f. exper. Path. u. Pharmakol.* **78**:1914). The circular states that Elarson contains about 13 per cent. arsenic. Joachimoglu found from 10.8 to 11.1 per cent. to be present. The circular states further:

> "The fact that Elarson represents a lipoid-like chemical combination of arsenic has an important bearing upon its absorption and utilization in the system . . . there is good reason to believe that when arsenic is administered in a stable, lipoid-like combination, as in Elarson, it is more readily taken up by the cells and more completely utilized than when given in the customary manner."

> "As regards the behavior of Elarson in the system, it has been shown that its active constituent, chlorarseno-behenol, is almost completely absorbed in this form, probably as a chlor-behenolate of sodium or potassium."

As a matter of fact, Joachimoglu found that very little arsenic was absorbed when Elarson was given to dogs and rabbits; most of it was recovered from the feces; only traces were found in the liver and kidneys and none in the blood and brain. The absence from the latter organs shows that the lipoid solubility does not obtain in the body. It is claimed in the circular that Elarson has the advantage over Fowler's solution "in that it is free from any irritating action upon the gastro-intestinal tract"; it is stated that as many as sixty tablets have been given to dogs daily without any toxic effects. Joachimoglu, on the other hand, found powdered

Elarson to be very irritating to the gastro-intestinal tract; also that the dog could not stand sixty tablets at all (*gar nicht vertragen*), such doses causing vomiting, diarrhea and intestinal hemorrhages; on repeated administration the symptoms became progressively more severe. Joachimoglu also found that, compared on the basis of arsenic content, Elarson, given intravenously, is from ten to twelve times as poisonous as arsenic trioxid. Elarson is recommended for the class of cases in which Fowler's solution is used.

To sum up: None of the special claims made for Elarson—the arsenic content, ready absorbability, freedom from irritating action on the gastro-intestinal tract and its alleged better adaptation for continued administration—have been substantiated; on the contrary, they have been disproved as well as the theory of its mode of absorption proposed by Fischer and Klemperer. Furthermore, Joachimoglu found that when it actually got into the circulation (intravenous injection) in the form in which Fischer and Klemperer supposed it to be absorbed, it was from ten to twelve times as toxic as arsenic trioxid.

The Council voted to omit Elarson from New and Nonofficial Remedies because it is sold under unproved and consequently unwarranted claims and because it is an unscientific and relatively useless article. Elarson has not been shown to have advantages over Fowlers solution; on the contrary, in some respects at least, it is inferior.

FORMICIN OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report announcing the omission of Formicin from New and Nonofficial Remedies.

W. A. PUCKNER, Secretary.

Formicin, manufactured by Kalle and Co., A. G. Biebrich a/Rh, Germany (Kalle Color and Chemical Co., New York, U. S. agents), was admitted to New and Nonofficial Remedies in 1912 with the following statement of its use:

"*Actions and Uses.*—Solutions of formicin liberate formaldehyde gradually at body temperature, and thus exert an antiseptic action. It is said to be non-toxic, and 5 per cent. solutions are said to produce but little irritation.

"*Dosage.*—Solutions of from 1 to 5 per cent. are employed as injections into tuberculous and non-tuberculous joints, tissues and abscesses; for bladder irrigation in chronic cystitis 2 per cent. solutions are used; 5 per cent. alcohol solutions have also been suggested for the disinfection of the skin and hands."

In 1918, the following report was adopted by the Council and sent to the Kalle Color and Chemical Company:

"The period of acceptance for Formicin has expired.

"The claims in the description in the 'Pharmaceutical Preparations of Kalle and Company' are practically those recognized in N. N. R. However, it is the opinion of the referee that further experience has not established the usefulness of Formicin.

Formicin is formaldehyd-acetamide, said to split off free formaldehyde gradually at body temperature. This gradual liberation was intended to avoid irritation. An antiseptic effect from non-irritant quantities of formaldehyde is only conceivable if there is a practically continuous supply of fresh formaldehyde liberated. That was doubtless the intention of the introducers of Formicin. However, such a continuous supply could scarcely be expected from a single or occasional injection of dilute Formicin solution into joints, fistulas, abscesses or bladder.

"The 'literature' as quoted in the pamphlet contains only three titles. These cannot be considered adequate evidence of its value.

"It is recommended that Kalle Color and Chemical Co. be asked to submit acceptable evidence of the usefulness of Formicin; and if this is not furnished that the substance be omitted from N. N. R. as in conflict with Rule 6 (unwarranted therapeutic claims)."

In reply, the Kalle Color and Chemical Company wrote in part:

"Our source of supply has supplied us with literature giving evidence of the value of Formicin. Due to the war we have been unable to get the latest pamphlets and it is impossible for us to submit acceptable evidence at this time.

"We should regret very much if under the prevailing conditions your Council should decide that 'Formicin' must be omitted from N. N. R. We sincerely hope that you can see your way to keep it on your list and reach your decision at such a time after the war when we have been able to supply you with additional evidence."

In view of this request and with the condition that the advertising to which objection was made be no longer distributed, the Council retained Formicin in New and Nonofficial Remedies in order that the firm might have the opportunity to present evidence for the value of Formicin.

The forgoing report was again brought to the attention of the Kalle Color and Chemical Company in August, 1919.

In order that the acceptability of Formicin for New and Nonofficial Remedies, 1920, might be determined, the report was again brought to the attention of the Kalle Color and Chemical Company with the explanation that the product

would be dismissed automatically from the next edition of the book if no acceptable evidence on the points raised in the report was available by Oct. 1, 1919. At the request of the Kalle Company, this time was extended by the Council to Jan. 1, 1920. However, no evidence was received and, accordingly, Formicin has been omitted from New and Non-official Remedies.

FRIEDLANDER BACILLUS VACCINE OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report.

W. A. PUCKNER, Secretary.

REPORT OF COMMITTEE ON SERUMS AND VACCINES

The following report was submitted by the Committee on Serums and Vaccines:

The referee has examined the available evidence on the use of bacterial vaccine made from the Friedländer bacillus, and has become convinced that such vaccine is without value.

It appears further that the only firm whose vaccine is at present in N. N. R. has also come to the same conclusion and has discontinued its manufacture.

It is therefore recommended that Friedländer bacillus vaccine be deleted from N. N. R.

ACTION OF THE COUNCIL

The Council adopted the preceding report and directed omission of Friedländer bacillus vaccine from New and Non-official Remedies.

HÉLÉNINE AND GLOBULES OF "HÉLÉNINE DE KORAB"

Report of the Council on Pharmacy and Chemistry

The Council has adopted and authorized for publication the report which appears below.

W. A. PUCKNER, Secretary.

Globules of "Hélénine de Korab" were submitted to the Council by Dr. De Korab Bojemski of Paris. According to the label, each globule contains 0.01 (Grammes?) of "Hélénine" and 0.005 (Grammes ?) of "Thébaïnée." A speci-

men of "Hélénine de Korab," which is claimed to be a derivative of elecampane and to be the chief ingredient in the globules, was also sent.

The major portion of the literature submitted with the globules consisted of a brochure, which was printed in 1889. This is devoted principally to the exploitation of "Hélénine de Korab," in respiratory affections, such as tuberculosis, chronic bronchitis, bronchopneumonia, asthmatic catarrh and engorgement of the lungs. Quotations are given from a number of medical journals of the early eighties, but these appear to be for the most part reading notices lauding the De Korab proprietary preparation, rather than accurate accounts of carefully conducted clinical trials with isolated "hélénine."

One of the claims made in the circular which accompanies the trade package of the Globules of Hélénine de Korab is that the preparation destroys the tubercular bacillus. (". . . détruit les microbes (stérilise les bacilles) de la tuberculose"). Many other therapeutic claims are exaggerated and unwarranted. Of late years, no attention appears to have been paid to "helenin" (from *Inula Helenium*) by medical men, either in France or elsewhere, the last therapeutic reference that was found having appeared in 1895.

The status of "helenin" as a therapeutic agent was discussed in a Council report in *The Journal of the American Medical Association,* Jan. 27, 1917, p. 303, and attention called to the dangerously misleading claim for "helenin" as a destroyer of tubercule bacilli.

Considerable confusion exists concerning the identity of the various substances called "helenine" or "helenin." From the roots of *Inula Helenium* (Elecampane) three distinct chemical substances have been isolated, to each of which, at one time or another, the name "helenin" had been applied. Further, the name "helenin" has also been given to a substance found in a different plant, *Helenium autumnale* (sneezeweed). The pharmacologic properties of the latter substance have been investigated by Lamson (*J. Pharmacol. & Exper. Therap.* **4,** 1913; editorial, *The Journal,* Nov. 15, 1913, p. 1819), who finds that it is a strong cardiac depressant and that it has very marked action as a local irritant.

From the literature submitted by Dr. De Korab Bojemski, it is impossible to identify the "hélénine" of his preparations with any of the substances to which the name "helenin" or "helenine" has been applied in modern chemical literature, although it is clear that the substance claimed to be used by him is derived from Elecampane (*Inula helenium*). The

brochure submitted with the globules gives the formula for "Hélénine" as $(C_6H_8O_2)N$ and this formula is given on the label of the trade package; whereas the formula now commonly assigned to the substance to which the name "helenin" is generally applied is $C_{15}H_{20}O_2$. The brochure further states that "hélénine" melts at 72 C., although modern authors state that the melting point of the substance having the formula $C_{15}H_{20}O_2$ is 115 C. The substance submitted melted between 65 and 69 C., but the melting point was not sharply defined.

Globules du a L'Hélénine de Korab is ineligible for New and Nonofficial Remedies because the composition of the Hélénine contained in Globules is indefinite; because the label advertises the product to the public (for use in bronchitis, asthma and grippe); because the therapeutic claims are unsubstantiated and unwarranted, and because the name of the product does not declare the potent constituent, thebaine.

HEMABOLOIDS OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The following report explaining the omission from New and Nonofficial Remedies of Hemaboloids has been authorized for publication.

W. A. PUCKNER, Secretary.

Hemaboloids (The Palisade Manufacturing Co.) is described in New and Nonofficial Remedies, 1918, as:

"A liquid said to contain, in each 100 Cc., iron, combined with proteins, equivalent to 0.40 Gm. elementary iron, proteins and nucleoproteins (nitrogen x 6.25) 4.0 Gm., bone-marrow extract 5.0 Gm., nuclein 0.04 Gm., in a menstruum containing 17 per cent. alcohol by volume."

The term of acceptance having expired, the Council voted to omit this preparation for conflict with Rule 10:

1. Because it contained red bone-marrow extract, which is no longer accepted for New and Nonofficial Remedies, because the experimental and clinical experience with that product has shown it to be without value. For obvious reasons, the Council does not recognize a mixture that contains an unofficial ingredient found ineligible for New and Nonofficial Remedies.

2. Because clinical experience affords satisfactory evidence that iron is administered with advantage in simple form, rather than in mixtures containing alcohol and in fixed combination with other medicaments, such as nuclein and red bone-marrow extract.

INFLUENZA PROPHYLACTIC-LEDERLE

Report of the Council on Pharmacy and Chemisty

The Council has authorized publication of the report which appears below.

W. A. Puckner, Secretary.

Under the designation "Influenza Prophylactic-Lederle," the Lederle Antitoxin Laboratories market a bacterial vaccine prepared from *Bacillus influenzae, Streptococcus viridans, Streptococcus hemolyticus,* Pneumococcus Type I, Pneumococcus Type II and Pneumococcus Type III.

Arguing that "a vaccine prepared from the bacteria which were found to be the chief infecting agents in influenzal pneumonia should afford the greatest degree of protection against influenza and its complications," the Lederle Antitoxin Laboratories explain that "All the cultures used in the preparation of Influenza Prophylactic Lederle were isolated from cases of influenza in the recent pandemic" and that they "include the influenza bacillus of Pfeiffer; the four types of *Streptococcus hemolyticus* as classified by Dochez, Avery, and Lancefield; the Rosenow strain of *Streptococcus viridans,* and the Mathers coccus and other green-producing streptococci isolated at Camp Meade; also the three fixed types of pneumococci as originally classified by Dole.

As there was no evidence to show the therapeutic efficacy of this "mixed" vaccine and as a mixture of two or more kinds of organisms is accepted for New and Nonofficial Remedies only if there is satisfactory evidence that its therapeutic use is rational, the Council decided not to accept "Influenza Prophylactic-Lederle."

IODIPHOS

Report of the Council on Pharmacy and Chemistry

A report which appears below was sent Charles L. Heffner for consideration. No reply having been received, the Council authorized its publication.

W. A. Puckner, Secretary.

Iodiphos, marketed by Charles L. Heffner, Brooklyn, N. Y., is declared to contain ferric citro-iodine, 6 grains; calcium glycerophosphate, 8 grains; sodium glycerophosphate, 8 grains, and hypophosphorous acid, 2 minims in each fluid-ounce, and to present "the Metallic and Non-Metallic elements: Iron, Iodine, Phosphorous, Calcium and Sodium (each in separate Basic combination)."

According to the label, Iodiphos is "ALTERATIVE, TONIC, NERVINE and ANTITUBERCULAR" and is "For Treatment of BLOOD, NERVES and PULMONARY ORGANS." An advertising circular[1] asserts that "Iodiphos exerts its Physiological action rapidly in hardening of the Arteries, High Blood Pressure, Anaemia, Glandular Swelling, Neurathenia, Hypochondria, Phthisis, Bronchitis, Asthma, Pneumonia and as an Intestinal Antiseptic and Appetizer," and declares it to be "Indispensable as a Tonic and Restorative."

In the advertising circular it is averred that in the production of Iodiphos "Chemistry Again Aids the Modern Physician." Iodiphos is another instance when a decadent polypharmacy proposes haphazard medication and so obstructs the efforts of modern medicine to establish the use of single drugs to meet definite indications.

Iodiphos is inadmissible to New and Nonofficial Remedies because it is an irrational mixture of drugs sold with therapeutic claims that are unwarranted, and under a name which is not descriptive of its composition.

MERVENOL AND ARMERVENOL NOT ADMITTED TO N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the report which appears below, declaring Mervenol and Armervenol, marketed by the Hille Laboratories, inadmissible to New and Nonofficial Remedies.

W. A. PUCKNER, Secretary.

Mervenol is stated by the proprietors—The Hille Laboratories, Chicago—to be a hydrosol (colloidal suspension) of the sulphides of mercury and copper, containing sufficient sodium chloride to make it isotonic with blood serum, and "inert proteoid" and "carbohydrate" to stabilize the colloidal suspension: each cubic centimeter is stated to contain 0.005 gm. mercury, 0.0016 gm. copper, and 0.0016 gm. sulphur.

It is claimed that this preparation is of value in pneumonia, influenza, and other conditions and diseases requiring increased leukocytosis.

It is further claimed that the properties and therapeutic effects of this preparation are as follows: "Practically non-irritant; practically non-toxic; lower temperature, often

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1. After publication of the foregoing report had been authorized by the Council, a letter was received from Charles L. Heffner, advising that the distribution of the circulars has been discontinued.

crisis like; lower pulse, with better elimination; greatly accelerated recovery from Influenza; fewer Pneumonia complications; lower mortality rate in Influenza and Pneumonia; remarkable Leucocyte stimulation." Administration by mouth and by intramuscular and intravenous injection are advocated.

In the recent influenza epidemic, it is reported that therapeutic results of some value were obtained at the Great Lakes Training Station and at Fort Sheridan. The reports of certain medical officers indicate that this preparation seemed to have some effect on the course of pneumonia and influenza, on the temperature, and on the leukocyte count. But those conducting the experiments state that it was "absolutely impossible" to fulfil ideal conditions as to controls and other observations at the time the experiments were conducted.

So far as the Council knows, no effort has been made to determine the potent constituent, or constituents, of this preparation; whether the mercury, the copper, or the protein in the mixture was responsible for the claimed benefits is an open question.

These reports were given careful consideration, but it was decided not to accept this preparation because of (1) exaggerated therapeutic claims, conflicting with Rule 6 (aside from the report of its use in influenza and pheumonia at the Great Lakes Training Station and the Post Hospital at Fort Sheridan, which reports are of work done and observations made under conditions which did not permit careful controls, no evidence has been presented to the Council supporting the therapeutic claims) and (2) being an irrational mixture, conflicting with Rule 10—a mixture containing colloidal mercury, copper and sulphur with proteins and carbohydrates in addition, it is difficult to predict the changes which occur in such mixtures on standing.

Samples of Mervenol (two 1-ounce bottles) submitted by the manufacturer, June 5, 1919, were found when opened, Aug. 18, 1919, to have undergone decomposition. A very disagreeable odor had developed, the liquid was turbid, and a large amount of precipitate had formed.

Armervenol is stated by the proprietors—The Hille Laboratories, Chicago—to be a hydrosol (colloidal suspension) of "mercury-copper-sulpharsenite" containing sufficient sodium chlorid to make it isotonic with blood serum and "inert proteoid" and "carbohydrate" to stabilize the solution: each cubic centimeter is declared to contain 0.0025 gm. arsenic, 0.005 gm. mercury, 0.0016 gm. copper, and 0.0032 gm. sulphur.

The use of Armervenol as advised by the Hille Laboratories is the same as that of Mervenol, and in addition its use in syphilis is emphasized. The criticisms of this mixture are similar in every respect to those directed against Mervenol—the addition of arsenic introduces still another factor of uncertainty.

After investigating these claims, it was decided not to accept this preparation on the ground (1) that the therapeutic claims are unproved and unwarranted, conflicting with Rule 6, and (2) that the mixture is an irrational one, conflicting with Rule 10.

MORPHIN MECONATE OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report, which explains the omission of Morphin Meconate from New and Nonofficial Remedies.

W. A. PUCKNER, Secretary.

The referee in charge of Morphin Meconate reported to the Council that this salt apparently has no advantages over the established salts of morphin. As the period of acceptance of the Morphin Meconate preparations admitted to New and Nonofficial Remedies—Morphin Meconate-Merck and Tabloid Morphin Meconate-B. W. and Co.—expired this year, the referee recommended that Morphin Meconate and the accepted preparations be omitted unless the firms marketing the accepted brands were in a position to submit evidence that the drug was not an unessential modification of an established article.

In reply to an inquiry asking if they possessed any evidence to indicate that Morphin Meconate had any advantages over the Pharmacopeial morphin salts, Merck and Co., New York, wrote:

"Answering your inquiry of the 6th inst., we have not at hand any evidence of importance as to the therapeutic value of Morphin Meconate aside from that one may perhaps find in medical literature. The salt has, of course, been known for many years, but commercially has been a very minor one. We manufacture it in response to a demand that is very limited. Possibly the demand may be something of a guide as to its usefulness. We note the salt was introduced into New and Nonofficial Remedies more than ten years ago. It was no doubt thought valuable at that time. The Merck brand was accepted in 1915."

To a similar inquiry, Burroughs, Wellcome and Co., New York, replied:

"In reply to your letter of the 6th of August *re* Morphine Meconate, we have been advised by our Head office that they have no knowledge that this product posseses advantages over the other Morphin Salts, and this appears to us to be a medical question. The product which we have issued has been to meet the demand from physicians for same. The sale, however, is extremely limited."

As it appeared from these replies that Morphin Meconate has no established advantage over the better known morphin salts, the Council directed the omission of the salt and the accepted preparations from New and Nonofficial Remedies

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NORMAL PHENOL SERUM (CANO) AND METHYL-PHENOL SERUM (CANO) NOT ACCEPTED FOR N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has adopted the following statement declaring Normal Phenol Serum (Cano) and Methyl-Phenol Serum (Cano) ineligible to New and Nonofficial Remedies.

W. A. Puckner, Secretary.

No statement of the composition of these preparations was submitted to the Council and none appears on the labels of the trade packages. However, the advertising circular contains statements such as:

". . . normal phenol serum—phenol with methyl blue dissolved in anaphylactic serum . . ."

". . . a combination of human or horse serum with Phenol and Methylene-blue, thereby forming a new chemico-biologic product which he termed Methyl-phenol Serum or, chemically, Chloride of Phenol Thionin Tetramethylene-Seric."

"Methyl-phenol Serum is a chemico-biological product in which Phenol is the chief factor. Each ampule of 10 c.c. contains the therapeutic equivalent of 0.5 gm. (7.5 grains) of Phenol."

From the foregoing it appears that both preparations contain phenol and methylthionine chloride (methylene blue) and that the second does not contain methyl phenol (cresol) as the name would indicate.

No definite evidence for the value of these preparations is brought forward and even the manufacturer is constrained to caution, "We assume no responsibility for the therapeutic action of the serum. . . ." On the other hand there are a great many statements in the papers of Cano and his colleagues to which exception must be taken. Of these, from among many similar, the following statements are to be cited and commented on:

"Accepting that the gonorrheal infection gives systemic toxemia from absorption of the toxins . . ."

It is the general opinion that in the majority of instances there is no systemic toxemia.

"The technique of intraprostatic injection, whilst less simple than that of the intravenous, is by no means so difficult or complicated as to place it exclusively in the category of the urologist."

This obviously is an attempt to encourage the general use of these preparations and to minimize the necessity for careful study and special skill in their employment. It is most unwise for one to attempt intraprostatic injections unless he is specially trained in the technique of this procedure.

"This injection to be performed after the 5th or 6th intravenous injection of Methyl-phenol Serum. . . ."

Intravenous injections have a place in sane therapy only when the medicament to be so administered is of known composition and when evidence is available which gives assurance that definite results shall follow its use. In the absence of these conditions it is manifestly unwise and even unexcusable to employ any medicament in this manner, and its repeated use is reprehensible.

"Intravenous injection of Methyl-phenol Serum alternating with intravenous injectins of mercury should be given every 48 hours until infection is under control."

This quotation further emphasizes that the treatment, as advised, carries with it a certain element of danger.

"Methylene blue prevents the phenol from exerting its usual action upon the red blood corpuscles, and ensures rapid elimination through healthy kidneys. It preserves the antiseptic power of the phenol and prevents the phenol from interfering with the chemico-biological function of the white and red blood cells. The serum component favors chemotaxis, it strengthens bodily defense, it prevents anaphylaxis even in debilitated patients, and it replaces the resistance which has been impaired by the demands that have already been made upon it."

No evidence is submitted to substantiate these claims. It seems strange that phenol should lose its power and that this should be restored by the methylene blue.

"It has a refractory chemico-biological action, and exercises no vicious effect on the red blood corpuscles in the circulation, but, on the contrary, by its inoffensive presence, it wholly preserves all of the physiological properties of the blood."

What "a refractory chemico-biological action" is, is not clear, but there is no evidence that this preparation has any action which might be defined as "refractory chemico-biological," that its presence is inoffensive or that it wholly preserves all the physiologic properties of the blood.

"The treatment of gonorrhea by Cano's theory . . . is firmly based upon chemico-biological facts and accepted authoritative theories and bears the same relation to gonorrhea that intravenous injections of arsenicals bear to syphilis."

Quite an exaggerated and unwarranted statement. In the same way, objection is taken to the following quotations:

"Phenol administered intravenously in combination with methylene blue, to protect the red-blood globule, undergoes no change, and preserves all of its actual antiseptic effect on the gonococcus and its toxins as though employed in the test tube."

"When thus introduced into the human body its elimination is unique, effective, antiseptic, germicidal, being completely and exclusively thrown off through the kidneys in a period varying from one-half to twelve hours without local injury or disturbance to the general economy."

"Combinations of phenol are unstable, but they do have the advantage of mitigating direct action on the cells and globules. It is also known that ordinary phenol has a *coagulant action* on the albumins and an *oxidizing power* on the tissues, which power, if permanent, produces gangrene. By virtue of this dual action it therefore acts as a *modifier;* by its oxidizing power on the germ it is germicidal, and prevents the growth of the gonococcus; and by its coagulant power on the toxins it relieves paragonococcal lesions (mono- and poly-arthritides) and affections of the serous organs (endo- and pericarditis, meningitis), and some definite systemic disturbances, the pathology of which is often confused with that of other infections."

"Lymphocytosis is often persistent in some individuals in whom the internal secretions and the processes of assimilation and disassimilation are deficient; and because of the lack of these the organic physiological ferments are insufficient for the mechanism of nutrition and the phenomena of hematopoiesis."

Until proof is available showing that phenol, administered intravenously in the quantities employed in Cano's Normal Phenol Serum and Cano's Methyl-Phenol Serum, acts as a germicide and methylthionine chloride ("methylene blue") prevents the deleterious effects of phenol on the red blood corpuscles; that repeated intravenous injections of phenol and mercury are without danger; that there is no danger of anaphylaxis; that the physiologic properties of the blood are preserved by these medicaments; and, finally, that these preparations have an effect on gonorrhea and its complications, these substances, Normal Phenol Serum (Cano) and Methyl-Phenol Serum (Cano), are inadmissible to New and Nonofficial Remedies.

The following quotations taken from the circular are admissions that these preparations are not innocuous:

"That the economy will tolerate to a surprising degree substances directly introduced through the blood stream is now well known. By the intravenous injection of 10 c.c. of methyl-phenol serum we throw into the human body a massive dose of an alien substance. The immediate effect of this injection is upon the central nervous system. The recipient usually becomes either pale or suffused, he has a ringing in his ears, has a sensation of great altitude, and occasionally has a dryness of the fauces and a metallic or a garlic taste."

"In some patients secondary reactions occur in from one to four hours after injection. The phenomena we have observed in these secondary reactions are pronounced chill and rigor . . ."

There is no doubt that considerable harm may be done by the intravenous and by the intraprostatic administration of these preparations and until there is good evidence showing the therapeutic value of the treatment, the routine use of these preparations, except perhaps at hospitals in selected and well controlled and carefully guarded cases, is to be strongly discouraged.

When the foregoing statement was sent the Mulford Company for comment, the firm submitted a letter from Dr. Perry Townsend to the Mulford Company in which he declared that the results obtained with the Cano preparations had been satisfactory and without untoward results. In this letter, Dr Townsend proposed that a series of injections with these preparations be carried out under the observation of members of the Council and the supervision of Dr. Cano or himself.

The report of the Council, the letter from the Mulford Company and that of Dr Townsend were sent to a number of urologists for their opinion concerning this whole matter. It was explained that the referee held that no reason had been presented which would warrant the Council to depart from its customary procedure, namely, to require that clinical evidence be submitted in the form of published reports which permit investigation and verification by independent observers but that, before making further recommendation to the Council, he desired the opinion of urologists of recognized standing concerning the report submitted to the Mulford Company. All replies received approved the Council's position.

The following is one of the replies received:

Your letter in regard to Normal Phenol Serum (Cano) and Methyl-Phenol Serum (Cano) received. I wish to state that I have read the correspondence between the Council and H. K. Mulford Co., and in my opinion the referee and the Council are quite correct in their attitude in the matter. In my opinion I would emphasize the following:

(1) There is absolutely nothing about the remedies directed *specifically* against the gonococcus and no evidence to show that any action against them is obtained. As we know there are certain states of normal serum which are highly toxic and any normal serum from another animal will produce disturbances in man when injected intravenously —particularly if repeated. The addition of substances to serum normal or otherwise is apt to and frequently does, render that serum highly toxic! The substances added in the instances referred to—phenol and methylene blue are not in any way calculated to lessen the toxicity of serum. The element of danger existing in the indiscriminate use of serums intravenously is, in my opinion, increased by the addition of the substances mentioned, and it would be unwise to encourage the general use of any such remedies. Furthermore the products are condemned by the very evidence of the originators and their admissions are quite sufficient to deter anyone from using the products as they suggest.

As to the intraprostatic injections with the serums it does not at all meet my views: although the introduction of serums by this route have been frequently advocated and I have personally carried this mode out I cannot allow the impression to go out that it could be done in a routine manner—nor that no ill results could follow—for I have seen otherwise. Furthermore from theoretical standpoint serums need not be given in this way.

In consideration of the opinion expressed by the Council's consultants the referee recommended that Normal Phenol Serum (Cano) and Methyl-Phenol Serum (Cano) be declared

ineligible for New and Nonofficial Remedies because of conflict with Rule 6 (unwarranted therapeutic claims) without considering possible conflicts with other rules, and that publication of the report be authorized.

SOAMIN OMITTED FROM N. N. R.

Report of the Council on Pharmacy and Chemistry

Soamin is the name under which the firm of Burroughs Wellcome and Company sells its brand of sodium arsanilate. The Council directed the omission of Soamin from New and Nonofficial Remedies and authorized publication of the report which appears below after the proprietors of the product had declined to withdraw or suitably to revise the unwarranted therapeutic claims which it made.

W. A. PUCKNER, Secretary.

The proprietary brand "Soamin" of sodium arsanilate was admitted to New and Nonofficial Remedies several years ago at a time when the therapeutic value of arsanilic acid had not been definitely determined. Experience with this drug has shown that it is far more dangerous and also has a more limited field of usefulness than was at first recognized. The proprietors of the Soamin brand have continued to include in the list of conditions in which it "would seem" to be a "very effective agent" cerebrospinal meningitis and pellagra; in fact meningitis is the first in the list of conditions mentioned, syphilis the second and pellagra third. In support of their belief in the efficacy of the remedy in meningitis, three reports, published from six to nine years ago, are quoted. In one of these it is stated that two patients "were cured"; in another report, seven of eight patients in whom the clinical, but not the microscopic, diagnosis of meningitis had been made were reported as having recovered; in the third report, fifty-six of ninety cases were reported cured; in this larger series of cases the author neglects to state the method of administration. The firm quotes but one paper (which is a very uncritical report) in regard to pellagra.

It seems to the Council that the evidence of value of sodium arsanilate in these conditions (which are now treated by more rational methods) is too slight to justify the emphasis laid on it by the firm, especially as sodium arsanilate is admittedly a dangerous agent, several cases of blindness having been reported from its use.

For these reasons it was voted to omit Soamin from New and Nonofficial Remedies.

SOME MIXED VACCINES NOT ADMITTED TO N. N. R.

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report.

W. A. PUCKNER, Secretary.

The consideration of the following "mixed" vaccines was requested by F. I. Lackenbach, San Francisco:

Special Bacterial Vaccine No. 2 (Staph-Strep. Bacterin) containing killed *Staphylococcus albus, Staphylococcus aureus* and streptococcus.

Special Bacterial Vaccine No. 3 (Pneumo-Staph-Strep. Bacterin) containing killed *Staphylococcus albus, Staphylococcus aureus,* streptococcus and pneumococcus.

Special Bacterial Vaccine No. 4 (Pneumo-Staph-Strep-Coli Bacterin) containing killed *Staphylococcus albus, Staphylococcus aureus, Staphylococcus citreus, Bacillus coli,* streptococcus and pneumococcus.

Special Bacterial Vaccine No. 5 (Influenza Combined Bacterin) containing killed *Staphylococcus albus, Staphylococcus aureus, Bacillus Friedländer, Bacillus influenzae, Micrococcus catarrhalis,* streptococcus and pneumococcus.

Special Bacterial Vaccine No. 11 (Pneumo-Strep. Bacterin) containing killed streptococcus and pneumococcus.

Special Bacterial Vaccine No. 15 (Combined Whooping Cough Bacterin) containing killed *Bacillus pertussis, Staphylococcus albus, Staphylococcus aureus, Micrococcus catarrhalis, Bacillus influenzae,* streptococcus and pneumococcus.

Special Bacterial Vaccine No. 16 (Mixed Gonococcus Bacterin) containing killed gonococcus, *Staphylococcus albus, Staphylococcus aureus, Bacillus coli,* diphtheroid bacillus, streptococcus and pneumococcus.

Mr. Lackenbach states that these bacterial mixture were prepared for him by E. R. Squibb & Sons. Their sale in interstate commerce is permitted under the license granted to the latter firm by the U. S. Treasury Department. However, no evidence of any kind was presented to the Council proving the therapeutic efficacy of the several mixed vaccines. As a mixture of two or more kinds of organisms is accepted for New and Nonofficial Remedies only if there is satisfactory evidence that its therapeutic use is rational, the Council declared the several vaccine mixtures ineligible for New and Nonofficial Remedies (Rule 10).

SOMNOFORM

Report of the Council on Pharmacy and Chemistry

The Council examined the available evidence for Somnoform, sold by Stratford-Cookson Company, successors to E. de Trey and Sons, and found the preparation inadmissible to New and Nonofficial Remedies. The Council authorized publication of the report which appears below.

W. A. PUCKNER, Secretary.

Somnoform is sold in the United States by Stratford-Cookson Company, successors to E. de Trey and Sons. According to the label on a package of Somnoform sent the Council,

"This mixture contains Chloride of Ethyl, 83 per cent.; Chloride of Methyl, 16 per cent.; Bromide of Ethyl, 1 per cent."

Although Somnoform has been on the market for a long time, the published reports present no proof that it is superior to ethyl chlorid used alone. Moreover, the published reports and statistics do not necessarily apply to the Somnoform now sold for the reason that mixtures of varying composition have been sold as Somnoform in the past. Thus, when Somnoform was considered by the Council in 1909, it was claimed to be composed of chloride of ethyl, 60 per cent.; chloride of methyl, 35 per cent., and bromide of ethyl, 5 per cent. Federal chemists found, however, that it contained no bromide of ethyl (Notice of Judgment No. 571). It is a question, therefore, whether a given report applies to a mixture containing 5 per cent. bromide of ethyl, 1 per cent. of this substance, or none at all

The present advertising booklet for Somnoform does not present acceptable evidence of the therapeutic value of the preparation. An ignorance concerning the elementary facts of physiology and pharmacology is evident in the second sentence: when having stated that "Somnoform is the result of several years of study and investigation by Dr. George Rolland, Dean of the Bordeau Dental School," the pamphlet continues: "He sought an anesthetic which would enter, dwell in, and leave the body in the same manner that oxygen does. . . ."

The claim as to the value of the 1 per cent. of ethyl bromide in the mixture is highly improbable; certainly no evidence in support of the claimed value of this constituent is available to the referee.

No evidence is submitted which proves the claim of superiority of Somnoform over similar preparations, asserted in the following:

"The peculiar manner in which the elements are combined is what makes Somnoform at once so efficient and so safe."

The Council declared Somnoform inadmissible to New and Nonofficial Remedies because, in the absence of acceptable evidence showing its exceptional safety and value, the claims are unwarranted (Rule 6), and because the name of the mixture is not descriptive of its composition (Rule 8).

TABLETS FORMOTHALATES

Report of the Council on Pharmacy and Chemistry

The Council has authorized publication of the following report which declares Tablets Formothalates (Tailby-Nason Company, Boston, Mass.) ineligible for New and Nonofficial Remedies.

W. A. PUCKNER, Secretary.

Tablets Formothalates are sold by Tailby-Nason Company, Boston, Mass. On the label a formula is given: "Constituents: Acetanilid 2 gr.; phenolphthalein ½ gr. In a balanced combination with Hexamene [a name sometimes applied to hexamethylenamin] and Oil of Cinnamon. Indications: Influenza, Colds, Grippe, Headache, Neuralgia, Rheumatism." The same formula is given in advertisements and in this advertisement it is claimed that they are "For Influenza and Grip" and if "given in the acute stage may avert a serious attack" (*Boston M. & S. J.*, Oct. 3, 1918). The dose is given as one to two tablets at 6 p. m. and repeat at bedtimes.

The A. M. A. Chemical Laboratory reported that the tablets weigh an average of 0.4882 Gm., or 7½ grains; that they *have* the odor and taste of cinnamon; and that they contain hexamethylenamin, are neutral and therefore give up no formaldehyde in the presence of water alone. The Laboratory further reported that they contain phenolphthalein and acetanilid. These tablets were directed to be taken internally and therefore their effect was not intended to be local.

The amount of hexamethylenamin was not determined, but in any case could not exceed 5 grains per tablet It is evident that 4 grains of acetanilid and 10 grains of hexamethylenamin and 1 grain of phenolphthalein (in two tablets) "if given in the acute stage" of influenza would not "avert a serious attack," as claimed in the advertisements.

The Council declared Tablets Formothalates inadmissible to New and Nonofficial Remedies.

TRIPLE ARSENATES WITH NUCLEIN

Report of the Council on Pharmacy and Chemistry

The Council has declared Triple Arsenates with Nuclein No. 1 and Triple Arsenates with Nuclein No. 2, tablets marketed by the Abbott Laboratories, inadmissible to New and Nonofficial Remedies because unwarranted therapeutic

claims (Rule 6) are made for them and because they present an illogical combination of drugs (Rule 10). The publication of the following report has been authorized by the Council.

W. A. PUCKNER, Secretary.

The following claims are made for Triple Arsenates with Nuclein:

"Puts 'pep' and strength back into that patient recovering from Spanish Influenza, pneumonia, typhoid, or surgical operation. An extremely powerful reconstructive tonic. Try it for that 'run down' feeling."

Triple Arsenates with Nuclein is said to contain "Strychnin Arsenate gr. $\frac{1}{128}$, Quinin Arsenate gr. $\frac{1}{64}$, Iron Arsenate gr. $\frac{1}{64}$, Nuclein Solution mins. 4." A second preparation, of double strength—Triple Arsenates with Nuclein No. 2—is also advertised. The Council voted not to accept these preparations for New and Nonofficial Remedies on the following grounds:

The quantities of quinin, iron and nuclein in the doses represented in these mixtures are negligible; thus, one tablet of Triple Arsenates with Nuclein containing $\frac{1}{64}$ grain of quinin arsenate contains only about $\frac{1}{90}$ grain of anhydrous quinin; the tablet containing $\frac{1}{64}$ grain of iron arsenate contains $\frac{1}{210}$ grain of iron; 4 minims of the nuclein solution (assuming it to be the "Nuclein Solution-Abbott") would contain but $\frac{2}{5}$ of a grain of nuclein—a substance which even in large doses is of questionable therapeutic value. The amounts of iron and nuclein contained in doses of this preparation are insignificant in comparison with the amounts present in ordinary foods. The only substances present in even small therapeutic doses are strychnin and arsenic. The effects of arsenic and strychinin are very different and there are comparatively few conditions in which they should be prescribed at the same time. Hence a preparation containing these two in fixed proportions is illogical.

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